

Control of airborne infectious disease in buildings: evidence and research priorities

Running title: Controlling airborne infection indoors

Authors: P. Jacob Bueno de Mesquita^{1*}, William W. Delp¹, Wanyu R. Chan¹, William P. Bahnfleth², Brett C. Singer^{1*}

Author affiliations:

¹ Lawrence Berkeley National Laboratory, Indoor Environment Group

² Pennsylvania State University, Department of Architectural Engineering

* Corresponding authors; jbueno@lbl.gov; bcsinger@lbl.gov

Abstract

The evolution of SARS-CoV-2 virus has resulted in variants likely to be more readily transmitted through respiratory aerosols, underscoring the increased potential for indoor environmental controls to mitigate risk. Use of tight-fitting face masks to trap infectious aerosol in exhaled breath and reduce inhalation exposure to contaminated air is of critical importance for disease control. Administrative controls including the regulation of occupancy and interpersonal spacing are also important, while presenting social and economic challenges. Indoor engineering controls including ventilation, exhaust, air flow control, filtration, and disinfection by germicidal ultraviolet irradiation can reduce reliance on stringent occupancy restrictions. However, the effects of controls—individually and in combination—on reducing infectious aerosol transfer indoors remain to be clearly characterized to the extent needed to support widespread implementation by building operators. We review aerobiologic and epidemiologic evidence of indoor environmental controls against transmission and present a quantitative aerosol transfer scenario illustrating relative differences in exposure at close-interactive, room, and building scales. We identify an overarching need for investment to implement building controls and evaluate their effectiveness on infection in well-characterized and real-world settings, supported by specific, methodological advances. Improved understanding of engineering control effectiveness guides implementation at scale while considering occupant comfort, operational challenges, and energy costs.

Practical Implications

Emerging variants of SARS-CoV-2 have led to increased infectivity by the aerosol inhalation mode and increasing infection incidence. Even in the absence of symptoms, people infected with respiratory viruses can exhale infectious aerosols that can be inhaled, deposit in the respiratory tract, and initiate infection. Indoor environments are the predominant settings for respiratory infection transmission because people spend most of their time indoors, and because concentrations of infectious aerosols can accumulate, resulting in hazardous inhalation exposure

at close-interactive, room (even at distances much greater than two meters), and building scales. We illustrate the relative respiratory aerosol transfer and exposure at these scales, provide an overview of the scientific basis of engineering controls that can be deployed in buildings to reduce transfer between people, and outline priority research directions to guide widespread implementation of controls in buildings.

Keywords

Infectious aerosols, COVID-19, ventilation, filtration, germicidal ultraviolet irradiation, engineering controls

Main Text

Introduction

When a pathogen has an important or predominant aerosol inhalation transmission mode, as is the case for SARS-CoV-2, shared indoor spaces pose elevated infection risk, and controls in buildings can mitigate spread^{1–5}. Emerging variants of the COVID-19-causing SARS-CoV-2 virus pose increased risk of aerosol inhalation transmission and reduced vaccine effectiveness^{6–10}, elevating the importance of non-pharmaceutical approaches in combination with vaccines to control the pandemic. Widespread use of face coverings and interpersonal distancing including quarantine, isolation, and occupancy restrictions in public and commercial places contributed to the control of COVID-19^{11–14}, and were relied upon to control the 1918–1920 pandemic^{15–17}. But, restricting interactions can cause harm to economic and educational development, and social wellness^{18–20}. Engineering controls—including ventilation (i.e., outdoor air supply), air filtration, and air disinfection with germicidal ultraviolet irradiation (GUV)—can reduce risk while enabling some in-person, communal activities.

COVID-19 transmission has occurred almost entirely in indoor settings of close congregation^{21–27}. Transmission from superspreaders, who may transmit to several or more others throughout their infection may drive community spread in public settings^{28,29}, while settings of small gatherings have also facilitated transmission²⁷. Exhaled aerosols that can carry infectious viruses, remain in indoor air for minutes to hours, and can rise to high concentrations in spaces without an adequate combination of ventilation and filtration. Although transmission risk is greatest between those interacting at close range, there can be substantial infectious aerosol transfer between people co-occupying an interior space even for a few minutes at nominally acceptable spacing (e.g., >2 m)³⁰. Despite their potential for societal health and economic benefits, ventilation and filtration standards for non-healthcare settings are not usually designed to control airborne infection³¹. Instead they have focused on reducing occupant dissatisfaction with odor and thermal conditions^{32,33}. Efforts to define a sufficient level of ventilation for infection mitigation are complicated by the range of effectiveness reported in the few available studies, and the inherent limitations in study methodology^{34,35}. Despite these uncertainties,

engineering interventions were recommended ^{1,3,30,36–43} and have been implemented in varied combinations in many buildings during the COVID-19 pandemic.

Engineering controls provide several key benefits. First, they are not reliant on knowledge of occupant infectious status as required for quarantine, isolation, and contact tracing. This is helpful because asymptomatic and pre-symptomatic COVID-19 cases were shown to shed at least as much virus as symptomatic cases and were estimated to contribute to a majority of transmission events ^{44–49}. Second, engineering controls reduce infectious aerosol exposure that can prevent infection, reduce severity of disease ⁵⁰, and possibly reduce subsequent propagation ⁵¹. Third, engineering controls provide some protection without having to address opposition to requirements such as masking or vaccination. Meanwhile, opposition to engineering controls centers on cost and energy use, and any individual control measure cannot achieve the benefits of an integrated set of controls that include the wearing of well-fitted masks and vaccinations for any who are able to access them once they are available. Fourth, increasing ventilation and improving filtration each bring substantial additional benefits, with ventilation improving cognitive performance ^{52–54} and reducing building-related illness and sick leave ^{55,56}, and filtration reducing a variety of health risks from exposure to fine particulate matter ^{57–59}. Fifth, infection resilience conferred through built environments helps address inequities in hazardous indoor exposures, and reduce inequalities in disease resulting from inequitable access to testing, personal protective equipment (PPE), or vaccination ^{60–64}. The reliance on school and business closures for infection control presents the greatest hardship to public-facing workers and communities who experience health, educational, and economic disadvantages ⁶⁵. Sixth, the societal benefits from infection control are expected to greatly outweigh the costs of implementing infrastructure upgrades ³¹.

Despite uncertainties along the aerosol infection pathway related to variations in the quantity of infectious pathogens shed into different aerosol sizes, sites of infection within the respiratory tract, variations of these factors by pathogen, stochastic effects, the physical dynamics of aerosols in buildings, and heterogeneity in population susceptibility, it is clear that viral aerosols play a driving role in respiratory infection, including for SARS-CoV-2 ^{1,66}. A recent study that detected infectious SARS-CoV-2 in fine aerosols ($\leq 5 \mu\text{m}$) from the exhaled breath of COVID-19 cases, showed that, controlling for viral load in upper respiratory mucosa, viral genome shed into aerosols was over an order of magnitude larger among alpha variant versus original “wildtype” infections ⁶⁷. This suggests that the SARS-CoV-2 virus is evolving to become more transmissible by the airborne mode, underscoring the importance of tight-fitting masks and respirators and airborne contaminant removal strategies in buildings. Research supporting the implementation and evaluation of engineering control measures on human infection and health outcomes is urgently needed in response to emerging SARS-CoV-2 variants and supports a better empirical understanding of the potential to reduce risk indoors. In recognition of the simultaneous and urgent need to reduce carbon emissions to slow climate change, the energy required to provide increased ventilation and air cleaning ^{68,69} motivates research to identify efficient practices that confer substantial infection control benefits ^{70–72}. To support widespread implementation of engineering controls, this manuscript presents a non-exhaustive summary of literature reporting intervention effectiveness, considered within a framework of exposure scales and settings, and proposes critical research aims and methods.

Sources, sizes, and transport of infectious aerosols

Infectious pathogens can be transferred between people in respiratory fluid via small, inhalable aerosols ($\leq 100\text{--}200\text{ }\mu\text{m}$ in diameter) and drops ($>100\text{--}200\text{ }\mu\text{m}$) that can deposit on facial mucosa but cannot be inhaled⁷³. Drops follow ballistic trajectories with momentum, often move independently of bulk air currents, and rapidly fall out of the air by deposition on surfaces. Particles with diameters below a few micrometers generally move with bulk fluid streamlines and have low enough deposition velocities that they mix similarly to gases, and are often removed from a room by ventilation and other processes faster than deposition⁷⁴. Aerosols up to $20\text{--}30\text{ }\mu\text{m}$ have low enough settling velocities that they remain airborne for several minutes or more and mix throughout an indoor space, driven by thermal plumes, HVAC air supply and other mechanisms of indoor airflow⁷³. Particles as large as approximately $60\text{ }\mu\text{m}$ can be kept aloft with typical room air speeds of $1\text{--}10\text{ cm/s}$, and particles up to $\sim 300\text{ }\mu\text{m}$ experience balanced flow conditions with air currents reaching 100 cm/s ⁷⁵.

Exhaled breath aerosols and drops containing water, salts, proteins, microbes and sometimes viruses are generated from several locations within the respiratory tract, resulting from the biophysics of breathing, vocalizing, or coughing^{73,76–80}. Based on a review of published studies, during respiration, a distribution of aerosols with number concentration modes $<1\text{ }\mu\text{m}$ in diameter are generated by the breaking of films that form in the lung airway reopening after closure^{75,81,80}. Shear forces and vibrations during vocalization generate aerosols from the throat region (larynx), with a larger size distribution and mode size of approximately $1\text{ }\mu\text{m}$ (ibid). Particles are also generated from the mouth with modes of 10 and $96\text{ }\mu\text{m}$ for vocalization, and 11 and $128\text{ }\mu\text{m}$ for coughing (ibid). In some studies, vocalization and coughing increased the average generated particle size by up to ten-fold^{78,82}. “Speech superemitters,” for reasons that are largely unknown, were shown to generate ten times more respiratory aerosol while talking than the study population mean ($N=48$)⁸³. Heavy breathing (e.g., with physical exertion), speech loudness, speech articulation, coughing, and singing have been observed to generate more aerosol particles than tidal breathing, likely due to changes in physical processes and greater expiratory volume^{83–86}. Presumably, laughing could present a different profile, though we are not aware of any studies quantifying emissions from this expiratory mode. Sneezing can release respiratory aerosols⁸⁷, and may be associated with some respiratory infections, however, was rarely observed in over 200 half-hour observational sessions from symptomatic influenza cases⁸⁸.

Virus-containing aerosols also can result from defecation and be spread via toilet use and from drain-waste vents. Wastewater sampling has been widely used as a research tool for population surveillance of SARS-CoV-2 infections^{89,90}. SARS-CoV-2 aerosols have been recovered in relatively high quantities from toilet rooms in hospital settings^{91,92}. Viral aerosolization from apartment building waste vents was epidemiologically implicated in the transmission of SARS^{93,94} and SARS-CoV-2⁹⁵. Vomiting is another potential source of infectious aerosols⁹⁶.

Studies of exhaled breath from infected humans are necessary to understand the quantity of pathogens released into aerosols of various sizes. The published body of such research over the last decade includes samples from several hundred individuals. These studies have reported higher pathogen loads in the aerosol fraction $\leq 5\text{ }\mu\text{m}$ in diameter compared with larger aerosols

⁹⁷. Influenza A and B viral genome copies (an indicator of the number of pathogens present) quantified from 218 exhaled breath samples from 142 symptomatic cases from a university campus community had a geometric mean three times higher in aerosols $\leq 5 \mu\text{m}$ versus $>5 \mu\text{m}$ ⁸⁸. Genome copies were correlated with infectiousness measured by quantitative culture (Spearman correlation coefficient 0.34, $p < 0.0001$). No association was found between viral quantity shed into exhaled breath aerosols (determined by Gesundheit-II bioaerosol sampling) and into upper respiratory mucosa (determined by nasopharyngeal swab samples), suggesting distinct compartments of infection in the upper and lower respiratory tract. A study of exhaled breath among a smaller population of symptomatic cases showed over eight times more viral genome in the fine versus coarse fractions (95% confidence interval 4.1–19) ⁹⁸. A similar pathogen load breakdown was observed in cough aerosols of influenza cases ⁹⁹: 65% of all influenza genome copies in the collected aerosol sample were recovered from particles $\leq 4 \mu\text{m}$ and almost twice as much was recovered from particles $< 1 \mu\text{m}$ compared with those 1–4 μm in diameter. A study of SARS-CoV-2 aerosols in exhaled breath during singing and talking from 22 asymptomatic to febrile COVID-19 cases detected viral genome in 59% of exhaled breath samples, with less shedding during breathing than talking or singing and a predominance in fine aerosol ($\leq 5 \mu\text{m}$) ¹⁰⁰. A study of 49 SARS-CoV-2 seronegative cases detected RNA in 45% of fine and 31% of coarse samples, and infectious virus in two fine aerosol samples despite the use of masks ⁶⁷. A paired analysis of masked and unmasked aerosol samples in this study showed that loose-fitting face masks reduced SARS-CoV-2 RNA in fine aerosol by 48% (95% CI 3%-72%) and in coarse aerosol by 77% (95% CI 51-89%). Given these findings, the authors emphasize the importance of tight-fitting masks, respirators, and air cleaning strategies, especially for protecting public-facing employees and those in crowded settings. The site of viral replication in the respiratory tract is expected to influence the particle sizes generated and lead to some variation in shedding sizes that could vary throughout the course of infection and between infection instances. However, there is substantial evidence that fine aerosols commonly carry infectious material that poses transmission risk via inhalation.

The size distributions relevant to airborne exposure assessment are those that result when infectious aerosols shrink by evaporation as they move from saturated conditions in the respiratory tract to indoor air with lower relative humidity ^{96,101–104}. Under common indoor conditions of $< 60\%$ RH, expired droplets rapidly evaporate to a final diameter that is approximately 20–40% of the starting diameter in the environmentally equilibrated form, sometimes referred to as droplet residua or droplet nuclei ^{75,101,105,106}. Aerosol droplet transport and diffusion distance after exhalation depends on the momentum (increasing from breathing to sneezing) of the multiphase turbulent cloud of exhaled air in which the aerosols are suspended and scales with the time from exhalation. The cloud decelerates and the aerosol concentration decreases as its growth entrains slower-moving ambient air ^{107–109}. Inhalation doses, therefore, decrease with distance from the infected person ¹¹⁰ and are dominated by aerosols $< 50 \mu\text{m}$ compared with larger aerosols and ballistic drops $> 100 \mu\text{m}$, unless the source was very close while talking ($\leq 0.5 \text{ m}$ away) or coughing ¹¹¹. Once the cloud's velocity is comparable to the velocity within the room (typically at $< 2 \text{ m}$), the ambient air currents dominate transport of the infectious aerosols ^{107–109}.

The sites of infectious aerosol deposition along the respiratory tract can influence the risk of infection and severity of illness. Larger aerosols deposit in the upper respiratory “head region”

and cannot reach the lower respiratory tract. Thoracic aerosols ($\leq 10\text{--}15\text{ }\mu\text{m}$) can deposit above and below the larynx. Respirable aerosols ($\leq 2.5\text{--}5\text{ }\mu\text{m}$) can deposit throughout the respiratory tract and more readily than larger aerosols in the lung^{73,75,80,112,113}. *Mycobacterium tuberculosis* must reach lung alveoli to initiate infection¹¹⁴. Influenza poses increased risk of infection and severe disease at lower doses when depositing in the lungs compared with the upper respiratory mucosa^{73,115}, and such anisotropic transmission may describe other infections. Although it appears that SARS-CoV-2 infection is possible throughout the respiratory tract based on the presence of relevant receptors¹¹⁶, the relative sensitivity to infection at different sites is unclear. An experimental challenge study of SARS-CoV-2 showed that cynomolgus macaques exposed to viral aerosols were more likely to develop fever and severe respiratory disease compared with those exposed to drops in the upper respiratory mucosa¹¹⁷. The effect was not observed in rhesus macaques, but nonetheless, suggests the possibility of aerosol inhalation as a sensitive mode of infection and important for control.

There are few field studies that have measured size-resolved pathogenic aerosols in buildings. An indoor air sampling campaign at an apartment showed a predominance of infectious influenza A in sampled aerosols with diameters $\leq 1\text{ }\mu\text{m}$ at 2 and 4 m from a bedridden case, with some infectious virus detected in particles larger than $1\text{ }\mu\text{m}$ at 1.2 m away¹¹⁸. Infectious SARS-CoV-2 aerosols with diameters <1.0 to $10\text{ }\mu\text{m}$ were recovered at 2 and 4.8 m away from hospitalized COVID-19 cases¹¹⁹. Other field studies have recovered viral genomic material in aerosols from a variety of settings. SARS-CoV-2 aerosols were detected in patient, staff, and public areas in hospitals⁹²; SARS-CoV-2¹²⁰ and influenza A¹²¹ in patient rooms; influenza A in a health center waiting area, a day-care center, and in airplanes¹²²; adenovirus and influenza A in a pediatric ward¹²³; influenza A in an emergency room¹²⁴; adenovirus, respiratory syncytial virus, and influenza A in metro rail cars¹²⁵; and influenza A in an elementary school¹²⁶.

In their seminal book on infection control, Riley and O'Grady hypothesized that pathogens with an important aerosol transmission mode, such as tuberculosis, evolved a level of resistance to infectious decay during residence time in the air between hosts¹²⁷. Laboratory quantification of infectious decay in rotating drums injected with aerosols containing influenza viruses, coronaviruses, and other viruses demonstrated infectious half-lives over an hour^{128–130}.

Psychrometric features could play a role in determining not only the fate of aerosol deposition and size change due to evaporation, but also aerosol infectious decay. A population-based study in Buenos Aires showed a correlation between reductions in relative humidity to approximately 60% and increased risk with a nine-day lag¹³¹. This relationship was only detected during the winter and did not rule out behaviors related to time spent indoors and indoor air ventilation. Despite this and other suggestions of increased viral aerosol decay in intermediate humidities^{101,132–134}, a study that aerosolized influenza virus from human respiratory tract cell lining fluid showed no effect of humidity on infectiousness during the course of an hour¹³⁵. A potentially protective effect of this lining fluid (the main component of exhaled breath aerosols) on infectious decay may be related to its chemical composition, compared with lab media used in other studies¹³⁶. Simulated saliva aerosols suspended in a rotating drum were shown to decay faster at 70% versus 20% RH at temperatures of $10\text{--}30^\circ\text{C}$; however, this effect was not clear under increased ultraviolet-B irradiance simulating sunlight¹³⁷. A commonly cited infectious decay rate of 0.63 h^{-1} comes from a study that aerosolized SARS-CoV-2 using non-human-based media in an aerosolization procedure likely to be more stressful than natural processes, leading to

potential overestimates when generalizing to human generated exhaled aerosol¹³⁰. Yet even if infectious decay were to occur at such a rate, it would represent a relatively small portion of total removal unless removal by ventilation is very low. Low relative humidity may be more likely to affect transmission by decreasing mucociliary clearance and innate immune function, as has been observed at 10% compared with 50% RH in mice¹³⁸. Yet, intentionally increasing humidity without careful oversight increases risks of dampness, mold, and other allergen exposures that are well established contributors to respiratory disease¹³⁹.

Critical scales and settings

The application and assessment of infectious aerosol controls indoors can be considered at three transfer scales: a) close-interactive, b) room, and c) building (between-room). Table 1 describes each scale and corresponding engineering controls. Administrative controls for all scales of transfer include pre-entry screening, face mask or respirator use as source control and PPE, activity limits (e.g., restricted loud speech, singing, or exercising), and frequent cleaning of common touch surfaces. Distancing tailored to setting-specific activities helps reduce close-interactive transfer. Limits to co-occupancy time, and cohort separation reduce room scale transfer. Distances 1–2 m have been commonly used to differentiate close- and long-range transmission along a continuum¹⁴⁰, related to likelihood of exposure to drops and aerosols. Features of close-interactive contact related to elevated airborne transmission have been described elsewhere^{141,142}. To differentiate between close-interactive—“garlic breath” scale of exposure¹⁴³—and room scale exposure we define close-interactive aerosol transfer within 1–2 m during a duration consistent with the US CDC’s definition of contact, which is 15 min or more within a 24 h period¹⁴⁴. A similar distinction in aerosol transfer exposure by proximity has been suggested by Nazaroff⁷⁵. Aerosol transfer from infectious to susceptible individuals within rooms is relevant when transport occurs much faster than deposition, removal, or viral inactivation. A modelling study predicted that the predominant scale of respiratory infection transmission can switch between close-interactive and longer-range, within-room exposures as a function of variation in infectious aerosol size, interpersonal distance, and exposure time¹⁴⁵. Increasing interpersonal distance within a room reduces the proportion of close-interactive transfer and increases the proportion of room scale transfer which is often more easily mitigated by ventilation, filtration, and GUV.

Table 2 lists features of settings that pose elevated risks owing to higher emission activities, limits on the applicability or ability to enforce administrative controls, or the likelihood that existing facilities have the equipment needed for engineering controls. Dining and sporting activities are less amenable to face mask wearing. Settings with higher occupant density, greater magnitude of interaction, and activity level present greater challenges relative to those with lower density and stationary occupants. Studies have implicated specific settings for SARS-CoV-2 and other respiratory infection transmission. These include school lunchrooms, restaurants, and small, private gatherings^{25,146}; classroom learning¹⁴⁷; a variety of occupational settings and worker dormitories²⁴; meat processing¹⁴⁸; religious services^{149,150}; public entertainment¹⁵¹; buses^{152,153}; nursing homes¹⁵⁴; and fitness centers^{155–159}. Residential settings, which typically foster extended exposure at close proximity, lend to transmission risk. A study of over 33,000 laboratory-confirmed influenza hospitalizations over two influenza seasons across the USA showed that having $\geq 5\%$ of people living in crowded households—defined as more than one

person per room—was associated with a 17% (95% CI 11-23%) increase in influenza hospitalizations, suggesting a possible role of within-household transmission in crowded environments ¹⁶⁰. A meta-analysis of household contacts estimated that spouses had a SARS-CoV-2 transmission rate of 38% (95% CI 26–51%) compared with 18% (12–25%) for other household contacts ¹⁶¹. Overall, the meta-analysis estimated within-household SARS-CoV-2 transmission risk of 16.6% (95% CI 14.0–19.3%) ¹⁶¹. Settings with immunologically susceptible populations and extended contact times include senior housing and assisted living communities, detention centers, homeless shelters, and healthcare settings. These settings may commonly have limited ventilation and air cleaning. Healthcare settings represent specialized environments with higher risks of exposure among and between patients and staff owing to increased sources of infectious aerosol ^{162–164}. Protection of immunologically susceptible patients is a priority and risk among staff is elevated with inadequate PPE and engineering controls ^{43,165–169}. Because of their unique exposures and elevated ventilation and infection control standards, healthcare settings are not a focus of this paper; however, many of the same controls applied in healthcare could be applied to other environments.

Community-level settings are likely to contribute to population transmission risk in unequal ways and this should be considered when assessing differential population exposure burdens in various settings. A study of US county level data showed that the effect of distancing policies on reducing COVID-19 cases and mortality was lower among communities of color, those with lower incomes, and those with higher levels of household crowding ¹⁷⁰, potentially related to cumulative exposure burdens related to built environment factors in occupational and residential settings. This is despite data that shows increased adherence to masking and physical distancing among Black and Hispanic communities in a national US survey, after controlling for socioeconomic status ⁶². Comprehensive, community-level prioritization of venues by risk level can be supported by risk estimation tools. For the purpose of minimizing overall spread and health impacts, priority intervention settings are those that serve as hubs for community transmission and those with populations that have higher risk of severe disease and adverse outcomes when infected.

Modeling risk and protective effects

Numerous tools have been developed to estimate SARS-CoV-2 aerosol exposure, infection risk, and the effect of controls in various indoor settings (Appendix 1). The Wells-Riley equation is often used to estimate risk of transmission at the room scale, where inhalation exposure and risk increase with the strength of infectious dose generation and decrease with removal via dilution ventilation and other mechanisms. The Wells-Riley equation is,

$$P = \frac{D}{s} = 1 - \exp\left(-\frac{I p q t}{Q}\right), \quad (1)$$

with P probability of infection, I number of infectors shedding pathogens into aerosols, q quantum generation rate, p pulmonary ventilation rate, t time sharing the air of an indoor space (assuming an evenly mixed environment), and Q uncontaminated air supply rate ¹⁷¹. The quantum generation rate, q , is the generation rate of inhalation doses, with one quantum defined as the dose that will cause infection in 63% of those exposed. It is estimated using data from outbreaks, based on the duration of shared air exposure between defined numbers of infectious and exposed individuals, the rate of removal by dilution or other means, and infection rates

among the total number of exposed susceptibles. Risk responds stochastically with a Poisson distribution proportional to the cumulative exposure to infectious aerosols. An infectious dose may be greater than a single, inhaled pathogen over the exposure period, but the likelihood of infection responds stochastically as though it were a single dose ¹⁷².

Rudnick and Milton built on the Wells-Riley equation by proposing the use of CO₂ concentration as a marker of how much air being inhaled in a room is composed of exhaled breath ¹⁷³. This works given that exhaled breath is the predominant source of CO₂ in indoor environments with vented combustion sources (e.g., cooking). Their rebreathed-air equation is,

$$P = \frac{D}{S} = 1 - \exp\left(-\frac{fIqt}{n}\right), \quad (2)$$

with n people sharing the air, and rebreathed-fraction f equal to the CO₂ concentration in the room minus the CO₂ concentration outdoors divided by the CO₂ concentration of exhaled breath—approximately 38,000 ppm at low levels of exertion ¹⁷³—integrated over the exposure time. Aside from providing direct estimates of exposure to exhaled breath (not accounting for removal via filtration, inactivation, and deposition) in a well-mixed room, and providing a solution for non-steady state conditions, the rebreathed-air equation can be used with data collected from CO₂ sensors, thus avoiding the challenges involved with estimation of room ventilation over time. Given a certain number of people occupying an indoor environment of a specified volume, the CO₂ concentration is a function of the rate of ventilation as outdoor air with lower CO₂ replaces indoor air containing exhaled breath. The transport of particles $\leq 3.5 \mu\text{m}$ has been shown to be well approximated by tracer gas ¹¹⁰. Although larger aerosols were not tested in that study, their dispersion would not typically be well-mixed and are likely to correlate less strongly with CO₂ concentration. The magnitude of this limitation is unlikely to negate the use of the rebreathed-fraction for practical, public health risk assessment in well-mixed settings, especially given the known importance of infectious aerosols $\leq 5 \mu\text{m}$ for transmission. Application of well-mixed, Wells-Riley based approaches to differentiate between close-interactive and room scale exposures has yet to be well explored ⁷⁵. Existing estimates of quanta generation rates are often given as population averages, yet they can vary widely between infector-susceptible pairs ^{174,175}. Precautionary approaches should consider superspreader scenarios as a function of supershedding, immunologic susceptibility, and elevated exposure to pathogen-laden air.

The Effective ReBreathed Volume (ERBV) builds on the rebreathed-fraction concept in a well-mixed space and provides a metric for characterizing infectious aerosol exposure as a result of transfer and removal processes occurring for aerosols of different sizes at various distances from a source ¹⁷⁶. ERBV characterizes exposure related to the physical transport of aerosols. This enables estimation of the influence of distance and filtration for aerosols across the range of relevant aerosol sizes. Improved knowledge of immunologically vulnerable sites along the respiratory tract (i.e., head, thoracic, and lung regions) by pathogen informs the risk implications of inhalation exposure of different sizes. Estimation of a person's cumulative inhalation exposure to infectious aerosols of various sizes would support improved assessment of aerosol infectious dose in well-characterized transmission scenarios. This would help with translating quantum generation rates into infectious aerosol copies per infectious dose, thus enabling aerosol sampling campaigns from human sources and/or indoor air to directly estimate risk in an indoor environment with known removal properties.

Insights from an aerosol transfer model in an office

To elucidate the importance of scale, we provide a quantitative example of aerosol transfer between an infected worker and susceptible workers at the three scales of exposure in an office setting (Figure 1; schematic in Figure A1). The simulation used CONTAM models of a single-zone (SZ) HVAC system serving a 92.9 m² room with an infected person, and a multi-zone (MZ) system serving 929 m² total floor area with at least two zones, one of which being the 92.9 m² infector room. Models were non-steady-state and the exposure lasted for one hour. All the spaces had 3 m tall ceilings and the HVAC systems supplied 0.47 L/s/m² (1 cfm/ft²) with 10% outdoor air, corresponding to 7.5 L/s/person of ventilation and 15 m²/occupant. Based on published data of exhaled breath aerosol size distributions, knowledge of the lung as a sensitive site for respiratory infection, and some uncertainty about sites of infection initiation along the respiratory tract for different infections, respirable aerosols $\leq 5 \mu\text{m}$ were included as relevant for infectious aerosol transmission along with thoracic aerosols $\leq 10\text{--}15 \mu\text{m}$ ^{73,102,82,177}. These sizes were environmentally equilibrated, achieved by taking 40% of emitted diameters⁷⁵ (listed in Appendix 2). Exploring this range of aerosol sizes allowed the model to show a quantitative estimation of relative exposure risk across scales of aerosol transfer. Despite the majority of exhaled breath and speech aerosol particles being $\sim 1\mu\text{m}$ ^{82,83}, and others showing a majority of influenza and SARS-CoV-2 virus in exhaled breath aerosols $\leq 5 \mu\text{m}$ ^{67,88,98,100}, a single particle at 10 μm or larger could potentially contain a greater viral load. It is unclear whether smaller aerosol particles might deliver fewer defective virions or facilitate binding to host receptors more readily than larger ones, but these possible explanations have been suggested for the detection of culturable SARS-CoV-2 in fine aerosol samples despite low viral load⁶⁷.

Close-interactive exposure is estimated as the aerosol number concentration at inhalation by a susceptible person whose head is within the same 1 m³ well-mixed subzone with the infected occupant. That subzone mixes with the surrounding room at a rate of 360 h⁻¹, corresponding to a mean air speed of 0.1 m/s. Mean exposures are considered at room scale, for susceptibles outside of the close-interactive zone within the infector room (Inf. room), with SZ or MZ systems, and at building scale outside the infector room served by the MZ system. If occupants are moving around the space, then local concentration extremes that can occur within a room are of less relevance as air becomes more well-mixed and occupants are exposed to air throughout the space. The effects of cloth face masks worn by both the infector and the susceptibles, are estimated in the simulation from size-resolved intake and out-flow removal efficiencies corresponding to a MERV 8 filter, consistent with published data on cloth masks^{178,179}. Out-flow efficiency considered aerosol sizes at emission, while intake efficiencies assumed aerosol sizes at equilibrium, which made breath aerosol filtration efficiency higher for exhalation than for inhalation. Additional sources of aerosol removal are dilution by outdoor air ventilation, deposition in HVAC ducts and on surfaces in the simulated rooms, and filtration by MERV 13 HVAC return filters (this example uses MERV 13, although $>\text{MERV } 13$ would be a reasonable approach also). The values of all model parameters and the differential equation that represents the material balance in the SZ infector room (as an example) are provided in Appendix 2. Results, shown in Figure 1, are presented as the ratios of hourly aerosol concentrations in the infector room and other rooms (building scale) relative to exposure concentrations within the close-contact sub-zone. The hourly, integrated number and volume distributions are shown in Figure A2 (Appendix 2).

The model represents an approximation of respiratory aerosol transfer. Aerosol number concentrations were highest at close-interactive scale (i.e., within the infector subzone), lower at room scale, and lowest at building scale (Figure 1; Figures A1, A2). It is possible that exposure could be even higher within the infector subzone compared with the other scales, depending on proximity of interaction of the individuals within the 1 m³ subzone and the dynamics of the exhalation plume from the infector which was not modelled in this scenario. Mask use among the infector and susceptibles reduced close-interactive exposure by 53, 97 and 98% for equilibrated particles with diameters of 0.3, 4.8, and 14.4 µm, respectively. Exposure reductions attributable to masking were similar for room and building scale transfer. Compared with the infector subzone, exposure concentrations in the infector room with an SZ HVAC system, without masking, were reduced by 79, 88, and 94% of those that occurred for 0.3, 4.8, and 14.4 µm, respectively. With masking, exposure was reduced further, to 90, 99.7, 99.9% of unmasked subzone levels. Compared with SZ, exposures in the infector room served by MZ HVAC were lower at the smallest particle sizes due to a greater supply of uncontaminated recirculated air, assuming no infectors in the connected spaces. Building scale exposure with the MZ system was dramatically lower than the other scenarios and declined faster as aerosol size increased. Other engineering controls could be applied to reduce exposure at the three scales (Table 1).

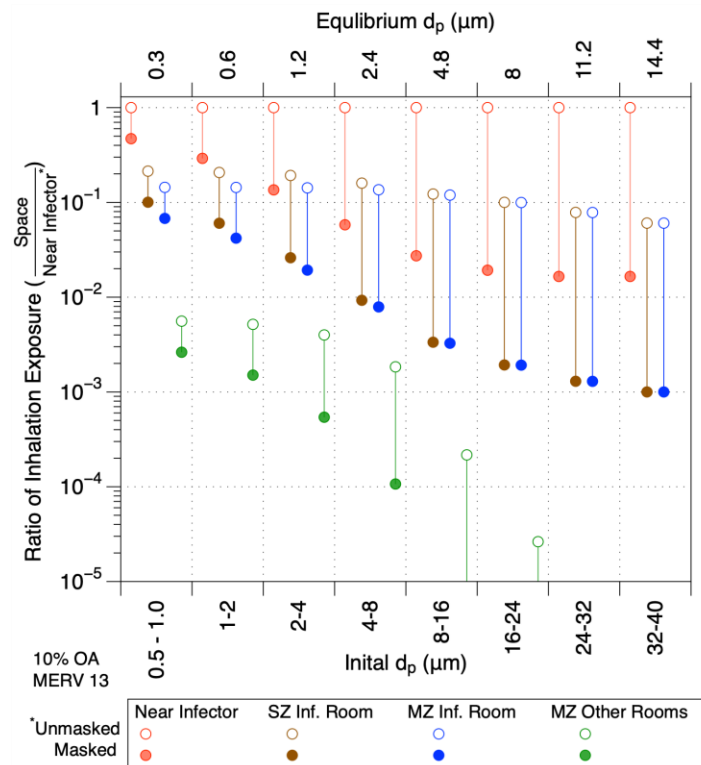


Figure 1. Relative inhalation exposure attributed to aerosols at different exposure scales compared with close-interactive exposure in the SZ Inf. Room. SZ Inf. Room = Single-zone HVAC system serving 93 m² with an infector in the room; MZ = mixed-zone HVAC system serving a total 929 m² with infector in the room; d_p = aerosol diameter; OA = outdoor air.

Intervention points to reduce infectious aerosol transfers

To support the prioritization of research needs, this section summarizes what is known about the efficacy of interventions to interrupt transfers of infectious aerosol. Source control measures and use of PPE are important measures in combination with the engineering controls and a brief description is included in Appendix 3.

I. Close-interactive scale

As illustrated in Figure 1, exposure at the close-interactive scale contributes the highest risk of aerosol transfer due to the contributions of concentrated aerosols close to the source and the possibility of large drop sprays. After more than a year of public information campaigns about transmission risk during close contact, there is broad awareness of the risk posed at this scale. Masking and distancing remain important controls at this scale, while airflow management and air cleaning at close range face implementation challenges at the population level.

Barriers

Although empirical effectiveness data are limited, a review of existing literature suggests that physical barriers such as plexiglass shields confer protection from ballistic drops and larger aerosols at close-interactive scale ¹⁸⁰, and may also help encourage physical separation between people. Physical barriers have been suggested in hospital settings to reduce between-patient and patient-visitor transfers and studied using computational fluid dynamics and tracer gas analysis ^{181,182}. Plexiglass-type shields deployed widely throughout an indoor space, such as between student desks in a classroom, may reduce exposure between adjacent individuals by increasing the distance for an aerosol to travel between people resulting in greater dilution potential. But they can also interrupt mixing and dilution ventilation, potentially leading to increased concentrations and exposures at some locations within room ¹⁸⁰. Rapid exhaust of air—at 114 L/s—above a fog-generating manikin reduced exposure between pupils seated next to each other at partitioned desks, however, the effectiveness of partitions under realistic classroom ventilation and air flow conditions may be low and could increase exposure due to interruption of dilution via air flow and mixing ¹⁸³. A thermo-fluid simulation using CO₂ tracer data to mimic the conditions of an office environment with plastic sheeting as shielding between groups of desks found that shielding likely reduced delivery of clean supply air to some spaces, leading to elevated risk ¹⁸⁴. A large-scale survey of pre-kindergarten through high school environments showed that classroom desk shields between pupils were associated with a 12% increase in odds of a positive COVID-19 test, and 29% increase in odds of COVID-19-like illness, after controlling for county infection incidence, and individual and household covariables ¹⁸⁵. Additional information about airflow, in this study or other classroom exposure scenarios, including where air enters and leaves the spaces and their interaction with barrier size and shape could help elucidate potential barrier-mediated airflow dynamics associated with risk and inform specific barrier use strategies to reduce risk. Settings where clean airflow delivery is not hindered by barriers such as at checkout registers in large market environments, could take advantage of protective effects of barriers without negative consequences.

Airflow management

Airflow management strategies to reduce direct transfer of infectious aerosol at the close-interactive scale include delivery of clean air directly to the breathing zone and establishment of beneficial airflow patterns. Directing expiratory air volumes toward upper-room GUV, into unoccupied volumes such as upper air spaces in high-ceilinged warehouses, or toward exhaust registers for in-duct cleaning and/or exhaust to outdoors can reduce between-person transfer. In general, mixing air improves performance of GUV¹⁸⁶. Directing air across a room would risk increasing the delivery of contaminated air from an infected person towards others in the space. The introduction of an uncontaminated airstream “curtain” between people was shown to reduce microbial contamination during surgical procedures¹⁸⁷, and could be applied to other contexts. An example of directed airflow around an infectious person is a ventilated headboard (such as that developed by NIOSH) that exhausts patient generated aerosols to reduce exposure to others nearby¹⁸⁸. Compared with a well-mixed space and the objective of cleaning the entire space, when room air is not well-mixed, provision of air cleaning and delivery close to the source can be more effective. This basic principle of air cleaning is well known and examples of the effectiveness of local air cleaning have been shown in recent studies^{189,190}. Although airflow and air cleaning measures can reduce close-interactive transfer when applied continuously, effective risk reduction strategies at this scale would benefit from addressing knowledge gaps about the distance and time required for source aerosols to dissipate to well-mixed levels within rooms.

II. Room scale

Exposure at room scale is important because of the potential for high concentrations of infectious aerosols, large numbers of exposed individuals, and prolonged exposure durations. Superspreading has been well-documented at this scale^{25,153,191,192}, and controls effective at this scale have the greatest potential to mitigate exposures and outbreaks at the community level^{28,29,174}. Room scale airflow controls offer greater protection at longer versus shorter range, and could offer better protection against respirable aerosols ($\leq 2.5\text{--}5\text{ }\mu\text{m}$) that are more easily entrained in air flow than larger aerosols and sprays with greater deposition removal¹⁴⁰. Transfer can be mitigated by ventilation, filtration, GUV, and air distribution to maximize control effectiveness (Figure 2). These approaches aim to reduce direct airflow connections between occupants, reduce well-mixed aerosol concentrations, and increase pathogen inactivation rates. There remain important research gaps in demonstrating the efficacy of individual room scale engineering controls and their effectiveness to reduce risk in population-based studies. Environmental quality and engineering controls in buildings are often not reported or their effects are not assessed in investigations of infection transmission. For example, two, high-profile population-based studies of SARS-CoV-2 transmission interventions in grad schools did not address the effects of controls like increased ventilation or air cleaner use because data on such controls was not collected^{185,193}, perhaps because there were no improvements in ventilation or infectious aerosol removal. There is a greater availability of evidence on controls that are commonly recorded such as distancing, masking, and symptom checks.

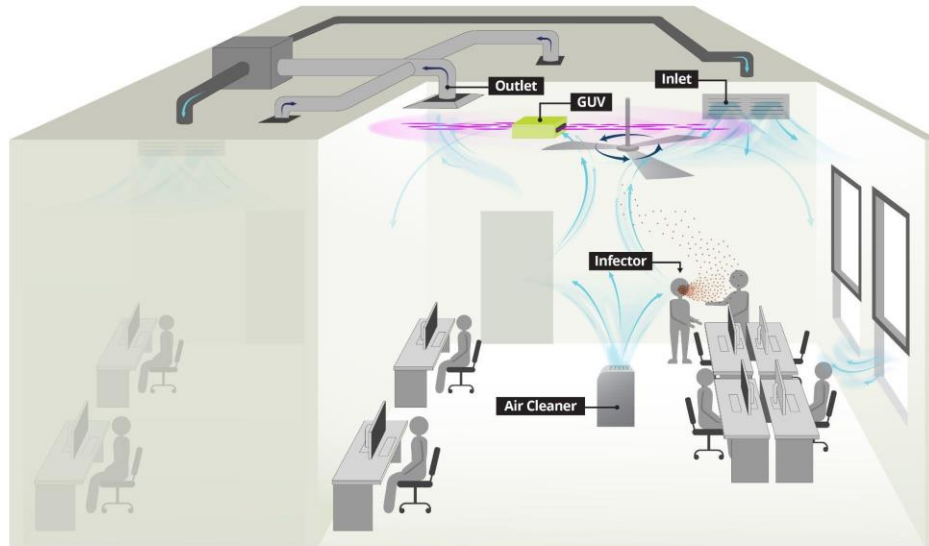


Figure 2. Scales of infectious aerosol transfer and control measures in buildings. Arrows depict airflow. Red dots depict infectious aerosols emitted from a single infectious person. These aerosols are likely to spread throughout spaces, beyond what is illustrated here, with relative exposures at different scales illustrated in Figure 1, however, control measures can reduce their transfer. Air flows in blue; GUV in light purple (although bluer in actuality when reflected off a surface).

Ventilation

In rooms that are well mixed, ventilation provides first order contaminant removal at the air exchange rate. Exposure reductions can be even higher with effective directional airflow patterns. Increased air exchange typically reduces exposure, unless a susceptible person is directly downwind of air flowing from the infectious source. Directional ventilation can reduce risk by controlling flows of potentially contaminated air¹⁹⁴. The importance of clean air supply for controlling infectious aerosols was described by both Nightingale and Billings in the 19th century^{195,196}, and by Wells in his foundational work in the mid-20th century¹⁷². Evidence from observational, experimental, and modelling studies supports the relationship between ventilation, occupancy, exposure time, and airborne infection rate^{171,173,174,197–203}. Systematic reviews have concluded that indoor ventilation levels are an important factor in airborne infection control^{34,35,204}. Without a more precise characterization of the effects of ventilation and other controls on infection risk, public health precaution supports an abundance of clean air delivery, which could potentially waste energy beyond what might be needed for infection control or other health benefits³⁰. A summary of how authoritative bodies have considered ventilation for infection control is included in Appendix 4.

There have been numerous case reports of respiratory infection transmission events in poorly ventilated environments. A report of nine secondary SARS-CoV-2 infections from a single primary case in a restaurant with recirculating air-conditioning units and an estimated ventilation rate of 0.9 L/s/p suggested a ventilation rate requirement of 38.6 L/s/p to inhibit transmission²⁵. Extensive transmission in poorly ventilated indoor environments contrasts with comprehensive contact tracing efforts that have detected very few instances of transmission during outdoor

exposures where dilution ventilation is abundant, as detected by comprehensive contact tracing efforts^{21,23,24,26,27,151,205–207}. When ventilation systems are limited in their capacity to increase the supply of outdoor air, some have suggested vacating indoor environments periodically to allow for air clearance^{208–210}.

Table 3 provides a summary of the main findings from a selection of epidemiologic studies that linked ventilation with respiratory infection risk. The studies included measured or estimated ventilation during exposure between primary and secondary cases, and calculated infection risk given an assessment of the total number of people exposed. Some were included in previous reviews^{34,35}. These studies consistently showed statistically significant increases in risk ranging from approximately 25–300% or more when comparing lower versus higher ventilation conditions. The generalizability of these existing studies is limited due to small sample sizes and designs that often fell short of achieving scrupulous exposure assessment and confirmed transmission under varying levels of well-characterized ventilation conditions. Human-challenge transmission studies in controlled environments with engineering interventions could provide stronger internal validity. External generalizability of such studies may be limited unless realistic exposure scenarios can be achieved. Human-challenge trials require substantial financial investment, careful design, execution, and attention to ethical concerns. A relatively large human-challenge influenza transmission trial failed to detect more than one transmission event, likely due to high ventilation rates in the quarantine facility in which it was conducted, and low infectious potential of the experimentally infected primary cases²¹¹. Other designs that test lower ventilation levels and/or draw from symptomatic, naturally infected populations could improve on this approach.

High ventilation rates of 6–12 air changes per hour (ACH) or more are often required in health care settings (Appendix 4) and can be achieved through natural and mechanical means²¹². Depending on the anticipated occupant density, minimum outdoor air exchange may be <1 ACH. When using natural ventilation, WHO suggested an hourly average flow rate of 160 L/s/p in airborne precaution rooms and 80 L/s/p (equivalent to 12 ACH in a 4x2x3 m space) in other health care spaces²¹³. This is consistent with total clean air flow delivery of 160 L/s/p in aerosol precaution spaces recommended by WHO interim guidance on COVID-19 infection prevention in healthcare settings²¹⁴. Natural ventilation is capable of achieving abundant air exchange but can also be much lower and is highly variable, dependent on wind speed, direction, and temperature. Window opening and natural cross ventilation in Peruvian hospitals resulted in air exchange up to 17 ACH in a consulting room and 66 ACH in a waiting room²¹⁵. Cross ventilation in a UK hospital achieved 27 ACH and uniform aerosol concentration across an open plan ward, given strong wind outside¹⁸¹. Natural ventilation can be influenced by the positioning of the room with respect to other building structures and thermal sources. Mechanically supplied ventilation can supplement low, natural, air flow delivery to assure an abundance of air exchange and mixing for infection control. Field studies of California schools found ventilation rates commonly below the ASHRAE standard of 7 L/s/p, suggesting the potential for widespread improvements in ventilation to meet standard rates^{216,217}.

Filtration

Filtration in recirculating HVAC units and in portable air cleaners removes respiratory aerosols, reducing exposure and infection risk^{218,219}. A 2020 ASHRAE position document states that filter efficiency of MERV 13 or better can effectively remove infectious aerosols²²⁰. MERV 13 filters

are rated to capture at least half of 0.3–1 μm , 85% of 1–3 μm , and 90% of 3–10 μm particles. If most of the infectious pathogens are contained in super-micron particles, then MERV 11 filters could provide comparable filtration efficiency. Compared with MERV 13 filters, they are less costly and tend to have lower air flow resistance, enabling higher airflows (and more air cleaning) or lower energy demand ²²¹. Filters with MERV ratings below 13 are not certified to capture submicron particles, but published filter performance evaluation indicates that MERV 8–12 filters can capture submicron aerosols ^{221–223}. Single pass filter efficiency typically increases with loading ²²⁴. Modeling studies of non-healthcare settings with various levels of assumed inhaled infectious aerosols have shown that air filtration in recirculating HVAC systems could decrease aerosol inhalation transmission ^{218,225}. A study of aerosol removal by four portable HEPA cleaners with a total 1026 m^3/h CADR (5.5 equivalent ACH) in an active classroom (128 m^3) with well-mixed air showed a 95% reduction in particles 0.01–10 μm after 37 minutes ²²⁶. Teachers and students indicated little disturbance by the noise of the air cleaners in the classroom, however, portable air cleaners can generate noticeable or uncomfortable noise levels in roughly the 50–60 dB range at maximum fan speed and ASHRAE has suggested selecting air cleaners based on reduced fan speed if noise is a concern ²²⁷. Do-it-yourself box fan cleaners with panel filters are generally noisier than commercial portable cleaners ²²⁸. It is clear that air filtration can reduce the indoor concentration of potentially infectious airborne particles when applied alone or in combination with other sources of contaminant removal via air exchange. Additional research could assess removal performance in a variety of real-world versus laboratory settings, effects on human health outcomes, and barriers to widespread use.

Germicidal ultraviolet irradiation (GUV)

Within-room infectious aerosol transfer can be controlled through the inactivation of pathogen infectivity using upper-room or far GUV. It is helpful to coordinate GUV use with airflow management to increase air movement to, and residence time in, zones of irradiance. GUV (sometimes abbreviated UVGI) has been used successfully for nearly a century to control airborne infections including *E. coli*, tuberculosis, measles, and influenza ^{175,229–235}. Upper-room GUV uses high energy, short wavelength radiation, within the UVC band of 200–280 nm, to damage the genetic material in viruses, bacteria, mold, and other organisms, rendering them noninfectious. Common GUV sources are mercury vapor or amalgam lamps that primarily produce ~254 nm UVC, which is close to the peak wavelengths for microbial inactivation (260–270 nm) with lower potential for skin or eye damage relative to longer wavelengths ²³⁶. More recently, LED lamps have been developed to produce similar wavelength with sufficient irradiance for disinfection ²³⁷. UVC is almost entirely absorbed in the outermost layer of the skin and is unlikely to pose cancer risk like longer wavelength UVA or UVB ²³⁸. A minor, yet painful irritation—erythema (skin) or photokeratitis (eye)—which normally resolves in 1–2 days, can occur from direct exposure prompting caution. The potential risk associated with eye exposure prompted the American Conference of Governmental Industrial Hygienists Committee on Physical Agents to assign a threshold limit value (TLV) of 6 mJ/cm^2 at 254 nm, however measured human exposures in a variety of healthcare and other workplace settings showed that exposure is generally far below the TLV, rarely reaching a third of the TLV at maximum ²³⁶. A trial of upper-room GUV (254 nm) at U.S. homeless shelters with thousands of staff and homeless participants found no difference in skin or eye symptoms between placebo and control periods ²³⁹. Exposure limits for a range of wavelengths provided by the International Commission on Non-Ionizing Radiation Protection (ICNIRP) reflects reduced penetration potential, and tests of 222 nm wavelength at a level seven times the ICNIRP resulted in no harmful effects in a

human skin model ^{240,241}. Environmental conditions and contact networks can influence the effectiveness of GUV controls at the population scale. GUV may have the greatest effect when applied in crowded, high-risk spaces. Interruption of aerosol transmission has been estimated to contribute to meaningful community-level infection control at hubs of human network connection, including when the inhalation mode accounts for as few as 20% of infections ^{199,200,242}. Lab-based studies of pathogen inactivation that assign “Z” or “k” rate constant values to indicate susceptibility to GUV facilitate estimation of inactivation rates across levels of exposure to GUV irradiance and under scenarios of varying humidity, air flow, and temperature ^{230,233,243–246}.

Upper-room GUV is typically installed on walls or ceilings to irradiate the upper zone of an indoor space. It has the advantage of rapidly treating large volumes of indoor air, making it highly efficient for infection control. Some studies have shown that, paired with a ceiling fan to increase air movement between the sanitization and breathing zones, upper-room GUV was capable of achieving an order of 10 or even 100 equivalent ACH ^{235,243,247,248}. The addition of a ceiling fan to stimulate air movement up into zones of upper-room irradiation was estimated to increase GUV-generated air change per hour equivalents by a factor of 2 or more ^{186,249}. Thermal plumes from occupants and objects in the room that are warmer than room air temperature (including e.g., any operating electronic equipment) create within room flow patterns of air moving into the sterilization zone in the upper part of the room then circulating back to the breathing zone along cold walls or cooler places without warm bodies. Wells and colleagues demonstrated that upper-room GUV substantially reduced transmission of measles, mumps, and chickenpox in suburban grade schools ^{234,250}. Subsequent epidemiologic investigations in other schools showed no significant effect, likely due to increased sources of transmission outside of schools in more urban settings ^{127,231}. Rates of infection in a Veterans Administration hospital deploying upper-room GUV during an influenza season were nearly 90% lower than those in nearby hospitals without GUV ²⁵¹. With regards to safety, upper-room GUV can achieve effective air disinfection while keeping exposure to irradiance, including that from reflections off ceilings, below workplace exposure limits ^{236,252}. Overall, the body of evidence supports upper-room GUV as an efficient and highly effective control against infectious aerosol transmission.

In-duct GUV can reduce within-room exposure during air recirculation to an extent similar to filtering recirculated air. A typical HVAC system in a non-healthcare application will supply approximately six ACH at most, and much less on average for a variable air volume system. Consequently, this is the maximum disinfected air delivery rate of such a system. On the other hand, upper-room systems can provide equivalent air changes much greater than six ACH. Nevertheless, both modeling and field measurements suggest that in-duct GUV can have cost-effective, beneficial health effects. Simulation of an in-duct system in three climates found that room air concentrations of pathogens were reduced by approximately 50-70%, with a median reduction of approximately 65% ²⁵³. A double-blind evaluation of GUV installed in office air handling units reported reduced levels of microbial contamination on air-handling unit surfaces and in the air, and lower levels of respiratory and other symptoms during GUV operation among 771 participating workers ²⁵⁴. An additional benefit of in-duct GUV, when done in an air-handling unit, is control of microbial growth on cooling coils and in condensate pans ²⁵⁵. Biofouling on cooling coils reduces air-side heat transfer coefficient and can reduce air flow or increase fan energy use. Recent field investigations report net energy use benefits of coil

irradiation as well as reductions in maintenance cost relative to mechanical and chemical cleaning^{256–259}.

Whole-room GUV floods the occupancy zone and can be useful for surface decontamination²⁶⁰; however, dust and crevices can provide shielding, thus reducing effectiveness. Thorough surface cleaning to access small crevices and remove particles may be warranted; and if an effective cleaning solution is used for that purpose, then additional disinfection may not be necessary. Depending on the wavelength used, it may be necessary to avoid exposure of skin and eyes to the whole-room GUV. Far GUV (UVC 200–230 nm) is designed to bathe occupied spaces with irradiance, leading to direct inactivation of infectious pathogens in the air or on surfaces within the occupied zone. Far GUV may have a similar capacity to inactivate microorganisms as the well-characterized higher UVC wavelengths (250–270nm), while reducing safety concerns with human exposure^{241,261}. Available studies using mammalian cell culture, animals, and humans have shown that 222nm far UVC can inactivate respiratory pathogens does not cause skin irritation associated with exposure to the 254nm wavelength^{241,261,262}. GUV “barriers,” or beams of germicidal light to sterilize air between office workers, have been used in the past with 254 nm sources, but safety concerns and declining TB rates in the US led to their disuse¹²⁷. Should further safety and efficacy evaluation of far GUV yield favorable results, far GUV could provide an update to GUV barriers of the past and contribute to infection control at room scale, and between infectious and susceptible individuals in close-interaction. Far GUV lamps can generate low levels of ozone, however, filtered lamps and lower power modes can ensure generation well below limits to protect health^{241,263,264}. Upper-room GUV applications that deploy wavelengths above 240 nm and block wavelengths below that do not produce ozone. Overall, with some care toward proper deployment to ensure effective and safe application, GUV can offer a helpful layer of airborne infection control, and perhaps a critical one in settings where other controls are not readily available.

Airflow management

Given that infectious respiratory aerosols are transported by air currents, air flow dynamics strongly influence transfer and intervention efficacy. Highly controlled laminar and unidirectional air flows can be used to reduce patient exposure to contaminants in operating theatres, and could be selectively adapted to high-risk, non-healthcare settings²⁶⁵. Experiments have been done to characterize air flow dynamics related to a variety of ventilation systems²⁰⁴. Although downward ventilation, displacement ventilation, mixing ventilation, and personalized ventilation influenced air flow in a room with a single patient, the investigators found that regardless of the type of ventilation, exhausting air at the top of the room represented a relatively effective means of removing aerosols, attributed to upward flow. Inlets positioned in the lower portion of the room to generate displacement ventilation can increase delivery of HVAC supply air to the breathing zone, although repositioning existing inlets may not be easy. A tracer gas study of aerosol exposure between stationary manikins ≤ 1.5 m apart showed that displacement ventilation was associated with lower time-averaged exposure compared with mixing or stratum air distribution²⁶⁶, consistent with what has been observed in previous modelling studies with intake fractions several orders of magnitude higher for ≤ 5 μm particles¹¹⁰. The effectiveness of displacement ventilation for removing exhaled breath aerosols can be diminished with increasing temperature gradients between the breathing zone and the upper zones of the room. Thermal stratification where air is warmer in the upper portion of the room compared with the air meant

to rise from the breathing zone can promote a locking effect of air within horizontal layers, thus reducing the rate of dilution^{267–269}. The addition of human movement throughout an indoor space promotes well-mixed conditions and, while helping to distribute infectious aerosol and reduce intense concentrations around a source, can also attenuate the speed of upward aerosol removal by a displacement ventilation scheme^{268,270}. Thermal stratification can also reduce effectiveness of systems intended to supply mixing ventilation, and is particularly problematic when the supply air is heated and provided at or along the ceiling^{271,272}. These potential problems with achieving maximum dilution ventilation spur future research directions. The addition of air currents and dispersion from human movement, portable air cleaners, and ceiling fans offer approaches to reduce thermal locking and increase mixing. This can help to deliver contaminated air more readily toward exhaust or GUV zones, and to deliver more clean air to breathing zones.

Deposition and control against resuspension

For respirable aerosols, deposition onto surfaces reduces airborne particle concentrations to a lesser extent than other mechanisms, and the extent to which deposition can be manipulated as an aerosol transfer control mechanism is limited. For aerosols larger than respirable size ($>5\ \mu\text{m}$) deposition is a major, if not dominant, source of removal. Deposition loss-rate coefficients in the range of approximately $0.1\text{--}7\ \text{h}^{-1}$ for particle sizes $0.55\text{--}8.66\ \mu\text{m}$ have been reported for a bare space with neither furnishings, occupants, nor mechanical air mixing^{273,274}. Surface deposition was shown to be increased by a factor of 1.3–2.4 by increasing airspeed from <5 to $19\ \text{cm/s}$ with fans, with a stronger effect on smaller particles²⁷⁴. However, compared with still air, some air movement from open windows or doors to the outside, mechanical systems, and occupants moving around can lengthen the airborne residence time. By adding $12\ \text{m}^2$ surface area via furnishings to a room with total volume $14.2\ \text{m}^3$, deposition increased by a factor of up to 2.6 with a stronger effect on larger particles (ibid). Studies of aerosols 1 to $>10\ \mu\text{m}$ introduced to HVAC ducts with typical velocities ($\sim 2\text{--}9\ \text{m/s}$) showed in-duct deposition increasing with aerosol size and velocity^{275,276}. Tests of aerosols $1\text{--}10\ \mu\text{m}$ in an HVAC coil apparatus showed up to 30% deposition, with increased deposition with aerosol size, and very mild increases in deposition with air speed change from $1\text{--}5\ \text{m/s}$ ²⁷⁷. The extent to which strategies to promote deposition can reduce infectious aerosol transfer in practice has not been extensively studied.

Once deposited on surfaces, potentially infectious material can be resuspended through disturbances, posing a potential source of transmission^{278–285}. Eight-hour room exposures to aerosols <1 to $>10\ \mu\text{m}$ were shown to increase by up to three orders of magnitude as a result of resuspended particles in an experimental HVAC duct²⁸⁶. Running HVAC systems for a “washout” period before occupancy can reduce exposure to particles that are re-aerosolized within supply ducts, and surface cleaning offers to reduce other sources of re-aerosolization. The infectivity of pathogenic aerosols that have settled and reaerosolized over various scales of residence time outside of hosts is not well characterized.

III. Building scale

Although building scale transfer is typically low, due to concentration dilution with distance from the source – including dilution within HVAC systems – (Figure 1), there exist scenarios where it could present non-negligible risk, with implications for populations larger than those at room scale. Air can be transferred between rooms by forced air HVAC, exhaust or pressure-

driven internal flows; vertically driven by stack effects and solar load; and horizontally driven by wind and temperature gradients. Beginning 20 years ago in response to the threat of weaponized anthrax, several modeling studies have presented strong evidence for building scale pathogenic aerosol transfer. A SARS superspreading event within a hospital ward was consistent with CFD showing the dispersion of airflow and aerosol viral concentrations from an infected person's cubical throughout an open ward^{287,288}. Similarly, a large MERS outbreak in a hospital was linked with airflow between patient rooms²⁸⁹. Detection of infectious MERS in the air outside of a makeshift MERS isolation unit suggested a failure of interzonal airflow control²⁹⁰. Beyond the healthcare setting, air flow patterns – constructed from tracer gas experiments, CFD, and statistical models – predicted the spatiotemporal distribution of SARS cases in a high-rise apartment complex, from a plausible source of viral aerosol from a plumbing vent, rising throughout buildings, and spreading across a courtyard to other buildings^{93,94,291}. Viral aerosolization from wastewater vents or natural ventilation air ducts has also been implicated in the vertical spread of SARS-CoV-2 in high-rise apartment buildings^{95,292,293}. In a university dormitory wing, multi-zone airflow modelling showed that the room of a resident with acute respiratory infection in the wing had an airflow connection with the only secondary case in the wing, suggesting a plausible aerosol transmission mode²⁰³. Although between-room connections within a house are generally different than between-room connections in a commercial or multi-unit building, available studies suggest that there could be more building scale transfer of submicron-sized aerosols within-unit than may be reported, missed by lack of investigation of between-zone connections.

Forced air thermal conditioning (HVAC) systems in commercial buildings typically mix air that is returned from the occupied zone with outdoor ventilation air. A common risk reduction recommendation early in the COVID-19 pandemic was to increase the amount of outdoor air and minimize recirculation²²⁰. ASHRAE Core Recommendations from several months later suggest that outdoor air supply meet code and the adoption of an effective clean air delivery approach²⁹⁴, consistent with parallel goals of energy savings and appropriate thermal conditioning. Filtration and inactivation by GUV within the HVAC system (along with deposition in the duct) can reduce infectious aerosol concentrations within and between rooms at much lower energy cost than outdoor air ventilation, which often requires thermal conditioning. An exception to this is the use of economizers, which, when outdoor conditions are suitable, increase the outdoor air fraction to achieve “free” cooling. Demand-controlled ventilation, on the other hand, reduces outdoor airflow in proportion to occupancy in order to save energy during periods when economizer operation is not possible, potentially increasing aerosol transfer. The risk associated with between-room transfer, although largely uncharacterized, would be greatly mitigated by the dilution that necessarily happens when air is mixed in an HVAC system serving a larger area (Figure 1). Nonetheless, air cleaning in-duct presents an opportunity for efficient pathogen mitigation contributing non-infectious air supply equal to the HVAC recirculation rates, which can often be as high as 4–6 ACH.

Building scale airflow interventions aim to reduce the magnitude of aerosol transfer from spaces with higher probabilities of infected people to spaces with susceptibles. Beyond healthcare settings, airflow management is especially relevant in residential environments where people spend extended periods of time and infected individuals are less likely to practice controls related to activities or masking. Yet knowledge on the efficacy of building-scale airflow interventions is

limited. A tracer gas study showing 2–35% transfer between-units in multiunit residential buildings showed sealing interventions resulted in a slight increase in median between-unit airflow²⁹⁵. Negative pressure, as deployed in hospital isolation areas, residential care, or household settings, can effectively move contaminated room air through an exhaust and reduce or eliminate exposure to individuals in the adjacent rooms or corridors^{194,296–298}. Yet such design strategies remain to be thoroughly explored for feasible translation, related to market and technician acceptance, in occupational, school, multiunit residential, and other settings.

Other benefits from infectious aerosol controls

Infection control has secondary health benefits beyond reducing acute disease. COVID-19 has resulted in numerous adverse sequelae including cardiovascular, brain, and long-term effects (“long COVID”)²⁹⁹. Reducing inhalation exposure to rhinovirus can lower the prevalence of severe asthma in children³⁰⁰. Elevated ventilation and filtration can lower exposure to dampness (related to climate), mold, and other indoor air contaminants of concern^{55,56,301,302}. Several studies reiterate the efficacy of filtration-based portable air cleaners for removing particulate matter as small as ultrafine ($\leq 0.1 \mu\text{m}$), associated with respiratory and cardiovascular disease^{303–307}. Cognitive function scores, work productivity, and performance on attention, speed, accuracy, and decision-making tests could also be improved with increases in ventilation^{52,54,308,309}. Several studies have documented reduced absenteeism in schools and workplaces with increased ventilation, related to reduced prevalence of respiratory illness^{54,217,310,311}. The costs of increasing ventilation are small compared with the health and wellness benefits in schools and workplaces^{31,312}, including in tropical climates where dehumidification costs are much greater³¹³. A 2002 multidisciplinary review estimated billions of dollars in economic savings in the US associated with health benefits from ventilation³¹⁴, an underestimate in today’s population and economic terms.

Research priorities

Knowledge gaps

Based on the reviewed literature, several key knowledge gaps have emerged that impede efforts to implement engineering controls for infection control, other health benefits. These gaps, posed below as questions, can be addressed through proposed research priorities in controlled and well-characterized environments, in real-world, practice-based settings, and through methodological advancements. A condensed version of knowledge gaps and research priorities is given by Figure 3.

1. For SARS-CoV-2, influenza viruses, and other respiratory pathogens, how much infectious virus is released through exhaled breath in aerosols of various sizes and what are the immunological, physiological, and activity-related predictors of infectious aerosol shedding? How many infectious virions are contained in individual aerosol droplets of different sizes, where are the most immunologically susceptible sites and population subgroups, and how do these factors influence infectious dose?

2. Given common configurations of airflow and patterns of human activity, how quantitatively heterogeneous is room scale aerosol concentration? How can controls reduce the distance between intense, close-interactive exposure, thus shifting exposure to the room scale that can be much more effectively controlled?
3. Which settings across societies represent the highest risk for aerosol inhalation transmission? To what extent do cumulative exposures, including environmental pollutants and psychosocial stress that are often unequally distributed across sociodemographic groups, mediate infection risk?
4. What advancements in modelling are needed to account for cumulative exposure to a range of relevant infectious aerosol sizes to provide substantially more specific estimates of infection risk? Which models can provide accurate estimation of engineering control effectiveness in a variety of real-world settings?
5. How can engineering controls be deployed in real-world environments (e.g., best configurations and combinations) to confer the greatest levels of protection? How can airflow management reduce close-interactive exposure and improve the effectiveness of ventilation, filtration, and GUV strategies? Which strategies can provide efficient evaluation and validation of emerging control technologies?
6. What arrangement of engineering controls can provide the greatest cumulative health benefits for the amount of energy required?
7. What strategies are most effective in facilitating implementation of engineering controls at scale given investment, operational, behavior change, and energy challenges related to adoption?

Research in controlled and well-characterized environments

Controlled experiments in well-characterized environments enable quantitative evaluation of intervention effectiveness in specific settings. Key elements include occupant positioning, spacing, movement, and interaction; airflows induced by human movement, natural or direct outdoor air mechanical ventilation, and forced air thermal conditioning systems; and common layouts, including open versus enclosed offices, large superstores versus smaller markets, configurations for congregant care facilities, table and seating arrangements in restaurants, etc. Better characterization of the physical properties and removal mechanisms of aerosols that carry infectious material would support the targeting of controls to specific pathogens, heterogeneous host populations, and the various indoor settings. The following activities would be particularly valuable.

1. Measure size-resolved infectious aerosol transfer (including respirable, thoracic, and larger aerosols) from human or simulated sources in relevant settings where masks cannot be worn (e.g., dining halls, restaurants) or where masks may not work effectively owing to activity or improper fit. Quantify the benefits of administrative and engineering controls in these settings.
2. Characterize the aerosol exposure dynamics differentiating close-interactive and room scale transfers, especially in environments that are not well-mixed and where connections between occupants vary widely with positioning, human movement, and use of barriers, intentional stratification, and other airflow management strategies. Identify effective controls for common configurations.

3. Conduct experimental studies to validate CFD modelling with the goal of supporting the development of simple, computationally tractable engineering models that can characterize within-room spatiotemporal evolution of infectious aerosol concentration. Identify modelling techniques that provide robust and practically informative results with acceptable computational burdens.
4. Quantify the effectiveness of controls such as portable filters and GUV (upper-room and far GUV) on aerosol and infectious agent surrogates in actual or simulated occupied buildings through controlled experiments, with particular focus on environments in which masks have limited applicability, people move around, or strict density limits have high costs (e.g., school hallways, grocery and retail, public transit, institutional dining, etc.). Studies are needed to characterize the performance of controls in generalizable ways (e.g., single pass efficiency of a filter) and then to quantify how the application of control measures under different conditions modulates performance (e.g., CADR in practice compared with nominal rating by AHAM test procedure).
5. Lower priority: Quantify potential transfers of infectious aerosols via resuspension from filters, floors, and other surfaces in rooms, and aerosol transfers between rooms, to address concerns that they could present significant risks under some circumstances.

Practice-based research

Practice-based research includes field studies and other investigations that support implementation of infection control measures targeted to specific settings.

1. Conduct retrospective, infectious disease outbreak investigations at sites where transmissions are suspected or confirmed to determine the transfer mechanisms (i.e., aerosols, direct transfer via drops, fomites), and build a knowledge base of the relationships between infection risk, exposure, and existing controls. Documentation of ventilation system configuration and operation and any extant filtration should be a standard part of outbreak investigations that cannot be entirely attributable to close contacts.
2. Invest in resource-intensive, population-based epidemiologic studies to improve understanding of the effectiveness of engineering and administrative controls to reduce exposure and transmission in specific settings. Study designs valuable to substantially advancing public health infection control include prospective infection monitoring with a) large populations (hundreds to thousands of participants) and crude evaluation of indoor environmental conditions including ventilation, filtration, or other features related to infectious aerosol transfer, and b) smaller populations and comprehensive characterization of indoor environmental quality and controls related to infectious aerosol transfer. The latter includes blinded interventions and sampling for infectious aerosols from environmental air and the exhaled breath of naturally infected occupants.
3. As is done for chemical hazards, conduct infectious aerosol transmission risk assessment using modelling that accounts for uncertainties in control effectiveness and variability in infectious dose generation rates associated with aerosol shedding, pathogen infectivity, and immunologically vulnerable exposed groups. To support risk assessment related to controls, develop algorithms to estimate the adequacy of outdoor and filtered air delivery when employing economizers, demand-controlled ventilation, or other dynamic systems, and evaluate associated energy savings.

4. Identify high priority settings for controls, including evaluation of exposure based on building features, use activities, socioeconomic features of building occupants and their cumulative exposures. Attention should be directed toward reducing exposures for socioeconomically disadvantaged communities and settings where building infrastructure facilitates elevated risk of transmission. Investigate the effects of winter minimum relative humidity—especially in cold climates—on health and vulnerability to respiratory infection.
5. Use research methods from social science and industrial engineering to systematically study the common challenges and barriers faced by building owners and operators who aim to implement recommended infection control guidance from ASHRAE, AIVC, CDC, WHO, etc. Challenges, listed below, may limit implementation or reduce control effectiveness.
 - a. Operational and energy-related challenges. Indoor air quality for thermal comfort and health and energy use are coupled; and increasing ventilation can increase energy use including peak demand. Achieving improved indoor air quality within the context of decarbonizing the built environment is an important need. Alternatives to ventilation or more effective ventilation are needed. The opening of windows to improve ventilation may complicate efforts to manage thermal comfort. There also exist challenges with achieving effective and reliable design and deployment of GUV given irradiance strength, room volume, and air flows.
 - b. Behavioral challenges. For example, controls that rely on human behavior, such as opening windows or manually-controlled mechanical ventilation or filtration systems, may not be implemented reliably or as intended. In some settings, open windows could increase exposure to ambient noise and air pollution, and could raise security concerns.
 - c. Institutional and financial challenges. Retrofits to upgrade HVAC equipment to improve ventilation or filtration may take years to implement. Those tasked with purchasing air cleaners may be influenced by sales pitches to buy higher cost units with unhelpful features and as a result not provide adequate coverage with conventional options. An example is high-priced portable air cleaners that utilize ionization but provide lower clean air delivery rates where devices with media filters could provide much more delivered clean air at lower cost.

Methods

The development and assessment of methods and metrics, listed here, supports priority studies in controlled and applied settings, including large-scale, prospective, transmission monitoring in buildings and control measure evaluation.

1. Develop metrics and supporting test methods for infectious aerosol inactivation. Methods should include surrogate viruses or organisms reflecting a range of pathogen susceptibility. The predicted effectiveness of exposure mitigation via GUV within a room currently requires complex modelling given knowledge of pathogen susceptibility. Metrics that enable estimation of the airborne infection control potential of GUV in combination with other controls would be particularly useful, including a CADR-like measure for infectious particle inactivation at different sizes. Metrics and methods (e.g., a chamber test procedure) can be used to evaluate efficacy of developing technologies

including those that release disinfectants into the air (e.g., ionization, hydrogen peroxide vapor, triethylene glycol) along with safety tests related to potential byproduct formation and health effects.

2. Develop methods to improve the sensitivity of infectious aerosol detection and quantification from exhaled breath and ambient air sampling. Improvements could be targeted for a) increased resolution of size-resolved aerosol collection, b) increased usability and accessibility of samplers to enable widespread use in research contexts and potentially also operationally in sensitive buildings, and c) recommended strategies to quantify aerosol pathogen loads in occupied buildings, considering sampling location, duration, and frequency.
3. Prepare computational models for use by building operators to estimate infectious aerosol inhalation exposure (e.g., via CONTAM) and energy demand (e.g., via EnergyPlus) as a result of individual or combined controls that consider the empirical assessment of a) expected transfer of aerosols of different sizes following release, and b) the in-situ effectiveness of control measures. The goal is to reduce the difficulty of working with multiple modeling tools and of generating appropriate validation data (e.g., well-mixed conditions to match CONTAM).



Figure 3. Knowledge gaps and research priorities to support implementation of indoor control measures against airborne infection.

Conclusions

Emerging variants of SARS-CoV-2 with increased transmissibility underscore the importance of controls for aerosol inhalation transmission. Ventilation, filtration, GUV, and airflow management can effectively reduce exposure to pathogenic aerosols in buildings, with

substantial public health benefit; but real-world demonstration and evaluation is needed to advance systematic and widespread implementation. Quantitation of viral shedding from study populations into saliva or upper respiratory mucosa have reported lognormal distributions^{48,315}, and few individuals shedding the most virus have been implicated in driving population transmission^{28,29}. If SARS-CoV-2 aerosol shedding across the population follows a lognormal distribution, as has been considered elsewhere³¹⁶, then controls that lower total viral aerosol exposure by a factor of 10 can approach a meaningful reduction in infectivity of the highest shedders by an order of magnitude, thus reducing the impact of supershedders and the chances of encountering someone shedding enough to pose transmission risk. Building-level, engineering controls provide opportunities to reduce reliance on the challenging physical distancing measures experienced during COVID-19 and other plagues. Engineering controls can add to risk reduction achieved by administrative approaches and thus support in-person gatherings that provide for social wellness, learning, and commerce. They also present an important opportunity to advance social justice in the wake of a pandemic with highly inequitable health and economic burdens.

This review identified gaps in existing knowledge that point to the need for studies and methods to measure, quantify, and model the relationships between control-mediated aerosol transfer and actual infection risk. We have built on previous reviews of engineering control effectiveness^{3,5,175,204} and contextualized priority research directions for evaluating controls at specific scales and settings. The goal is to support efforts to tailor and modify control measures akin to personalized medicine, based on the infectiousness of various pathogens of concern and based on the exposures hosted by the setting. Evaluation of implemented control measures must consider aerosol transfer mechanisms specific to the close-interactive, room, and building scales. The overarching research goal spurred by the COVID-19 pandemic is to inform infection controls that reduce risk to acceptably small levels, thus minimizing disruption of indoor activities, while also minimizing energy and economic impacts. We provide a framework for considering the physical processes governing pathogenic aerosol transfer, independent of pathogen infectivity and host susceptibility, which may be highly variable. This supports efforts to select setting-specific control strategies with well-predicted effects on aerosol transfer and energy requirements.

Data availability statement

The data that support the findings of this study are openly available in GitLab at https://gitlab.com/jacobbueno/building_controls_for_infectious_aerosols.

Author contribution statement

P. Jacob Bueno de Mesquita: Conceptualization (lead), Methodology (lead), Data curation (supporting), Supervision (equal), Formal analysis (equal), Visualization (lead), Writing-original draft (lead), Writing-review & editing (lead).

William W. Delp: Conceptualization (supporting), Methodology (equal), Data curation (lead), Formal analysis (equal), Visualization (lead).

Wanyu R. Chan: Funding Acquisition (lead), Conceptualization (supporting), Visualization (supporting), Methodology (supporting), Writing-review & editing (supporting), supervision (supporting).

William P. Bahnfleth: Conceptualization (lead), Formal analysis (supporting), Methodology (supporting), Writing-original draft (equal), Writing-review & editing (equal).

Brett C. Singer: Funding Acquisition (lead), Conceptualization (lead), Methodology (lead), Project Administration (lead), Supervision (lead), Formal analysis (equal), Writing – Original Draft Preparation (supporting), Writing – Review and Editing (lead).

Acknowledgements

We thank William J. Fisk, Linsey C. Marr, Mark J. Mendell, Carl Shapiro, Jeffrey A. Siegel, John E. Swartzberg, and Iain Walker for helpful feedback. We thank Cristen Farley for the illustration.

Funding

This work was supported primarily by the Commercial Building Integration program of the Building Technologies Office, within the U.S. Department of Energy's Office of Energy Efficiency and Renewable Energy, via Contract DE-AC02-05CH11231. Additional support was provided by the Indoor Environments Division of the U.S. Environmental Protection Agency via Interagency Agreement DW-89-9232201-7. The aerosol modeling work was supported by the U.S. Department of Energy Office of Science, through the National Virtual Biotechnology Laboratory, a consortium of DOE national laboratories focused on response to COVID-19, with funding provided by the Coronavirus CARES Act.

Conflict of interest statement

PJBdeM received fees from PandemicProof Productions for advising on strategies to reduce SARS-CoV-2 transmission during film production.

WB conducted air cleaner research at Penn State funded by ActivePure Technologies.

References

1. Greenhalgh T, Jimenez JL, Prather KA, Tufekci Z, Fisman D, Schooley R. Ten scientific reasons in support of airborne transmission of SARS-CoV-2. *The Lancet*. 2021;0. April 15, 2021. [https://www.thelancet.com/journals/lancet/article/PIIS0140-6736\(21\)00869-2/abstract](https://www.thelancet.com/journals/lancet/article/PIIS0140-6736(21)00869-2/abstract). Accessed April 21, 2021.
2. Prather KA, Wang CC, Schooley RT. Reducing transmission of SARS-CoV-2. *Science*. May 2020:eabc6197.

3. Morawska L, Tang JW, Bahnfleth W, et al. How can airborne transmission of COVID-19 indoors be minimised? *Environ Int.* May 2020:105832.
4. Yang B, Huang AT, Garcia-Carreras B, et al. Effect of specific non-pharmaceutical intervention policies on SARS-CoV-2 transmission in the counties of the United States. *Nat Commun.* 2021;12:3560.
5. Burridge HC, Bhagat RK, Stettler MEJ, et al. The ventilation of buildings and other mitigating measures for COVID-19: a focus on wintertime. *Proc R Soc Math Phys Eng Sci.* 2021;477:20200855.
6. Port JR, Yinda CK, Avanzato VA, et al. Increased aerosol transmission for B.1.1.7 (alpha variant) over lineage A variant of SARS-CoV-2. *bioRxiv.* July 2021:2021.07.26.453518.
7. Sheikh A, McMenamin J, Taylor B, Robertson C. SARS-CoV-2 Delta VOC in Scotland: demographics, risk of hospital admission, and vaccine effectiveness. *Lancet Lond Engl.* 2021;397:2461–2462.
8. Musser JM, Christensen PA, Olsen RJ, et al. Delta variants of SARS-CoV-2 cause significantly increased vaccine breakthrough COVID-19 cases in Houston, Texas. *medRxiv.* August 2021:2021.07.19.21260808.
9. Hetemäki I, Kääriäinen S, Alho P, et al. An outbreak caused by the SARS-CoV-2 Delta variant (B.1.617.2) in a secondary care hospital in Finland, May 2021. *Eurosurveillance.* 2021;26:2100636.
10. Fisman DN, Tuite AR. Progressive Increase in Virulence of Novel SARS-CoV-2 Variants in Ontario, Canada. *medRxiv.* July 2021:2021.07.05.21260050.
11. Bielecki M, Züst R, Siegrist D, et al. Social distancing alters the clinical course of COVID-19 in young adults: a comparative cohort study. *Clin Infect Dis.* 2021;72:598–603.
12. BSG Working Group. *Variation in Government Responses to COVID-19.*; 2020. September 1, 2020. <https://www.bsg.ox.ac.uk/sites/default/files/2020-09/BSG-WP-2020-032-v7.0.pdf>. Accessed May 13, 2021.
13. Koo JR, Cook AR, Park M, et al. Interventions to mitigate early spread of SARS-CoV-2 in Singapore: a modelling study. *Lancet Infect Dis.* 2020;20:678–688.
14. Vali M, Mirahmadizadeh A, Maleki Z, Goudarzi F, Abedinzade A, Ghaem H. The Impact of Quarantine, Isolation, and Social Distancing on COVID-19 Prevention: A Systematic Review. *J Health Sci Surveill Syst.* 2020;8:138–150.
15. Bootsma MCJ, Ferguson NM. The effect of public health measures on the 1918 influenza pandemic in U.S. cities. *Proc Natl Acad Sci U S A.* 2007;104:7588–7593.
16. Hatchett RJ, Mecher CE, Lipsitch M. Public health interventions and epidemic intensity during the 1918 influenza pandemic. *Proc Natl Acad Sci.* 2007;104:7582–7587.
17. Markel H, Stern AM, Navarro JA, Michalsen JR, Monto AS, DiGiovanni C. Nonpharmaceutical Influenza Mitigation Strategies, US Communities, 1918–1920 Pandemic - Volume 12, Number

- 12—December 2006 - Emerging Infectious Diseases journal - CDC. December 2006. December 2006. https://wwwnc.cdc.gov/eid/article/12/12/06-0506_article. Accessed July 14, 2021.
18. Cutler DM, Summers LH. The COVID-19 pandemic and the \$16 trillion virus. *JAMA*. 2020;324:1495–1496.
19. Hanushek EA, Woessmann L. The economic impacts of learning losses. September 2020. September 10, 2020. https://www.oecd-ilibrary.org/education/the-economic-impacts-of-learning-losses_21908d74-en. Accessed May 24, 2021.
20. Nicola M, Alsafi Z, Sohrabi C, et al. The socio-economic implications of the coronavirus pandemic (COVID-19): A review. *Int J Surg Lond Engl*. 2020;78:185–193.
21. Bulfone TC, Malekinejad M, Rutherford GW, Razani N. Outdoor Transmission of SARS-CoV-2 and Other Respiratory Viruses: A Systematic Review. *J Infect Dis*. 2021;223:550–561.
22. Frieden TR, Lee CT. Identifying and interrupting superspreading events—implications for control of severe acute respiratory syndrome coronavirus 2. *Emerg Infect Dis*. 2020;26:1059–1066.
23. Furuse Y, Sando E, Tsuchiya N, et al. Clusters of coronavirus disease in communities, Japan, January–April 2020. *Emerg Infect Dis*. 2020;26. June 10, 2020. https://wwwnc.cdc.gov/eid/article/26/9/20-2272_article.
24. Leclerc QJ, Fuller NM, Knight LE, Funk S, Knight GM. What settings have been linked to SARS-CoV-2 transmission clusters? *Wellcome Open Res*. 2020;5. June 5, 2020. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7327724/>. Accessed May 17, 2021.
25. Li Y, Qian H, Hang J, et al. Probable airborne transmission of SARS-CoV-2 in a poorly ventilated restaurant. *Build Environ*. 2021;196:107788.
26. Nishiura H, Oshitani H, Kobayashi T, et al. Closed environments facilitate secondary transmission of coronavirus disease 2019 (COVID-19). *medRxiv*. March 2020:2020.02.28.20029272.
27. Qian H, Miao T, Liu L, Zheng X, Luo D, Li Y. Indoor transmission of SARS-CoV-2. *medRxiv*. 2020:2020.04.04.20053058.
28. Endo A, Centre for the Mathematical Modelling of Infectious Diseases COVID-19 Working Group, Abbott S, Kucharski AJ, Funk S. Estimating the overdispersion in COVID-19 transmission using outbreak sizes outside China. *Wellcome Open Res*. 2020;5:67.
29. Adam DC, Wu P, Wong JY, et al. Clustering and superspreading potential of SARS-CoV-2 infections in Hong Kong. *Nat Med*. 2020;26:1714–1719.
30. Morawska L, Milton DK. It Is Time to Address Airborne Transmission of Coronavirus Disease 2019 (COVID-19). *Clin Infect Dis*. 2020;71:2311–2313.
31. Morawska L, Allen J, Bahnfleth W, et al. A paradigm shift to combat indoor respiratory infection. *Science*. 2021;372:689–691.
32. ANSI/ASHRAE. ANSI/ASHRAE Standard 55-2020: Thermal environmental conditions for human occupancy. 2020. 2020.

- https://ashrae.iwrapper.com/ASHRAE_PREVIEW_ONLY_STANDARDS/STD_55_2020. Accessed June 28, 2021.
33. Persily AK. Challenges in developing ventilation and indoor air quality standards: The story of ASHRAE Standard 62. *Build Environ*. 2015;91:61–69.
 34. Li Y, Leung GM, Tang JW, et al. Role of ventilation in airborne transmission of infectious agents in the built environment - a multidisciplinary systematic review. *Indoor Air*. 2007;17:2–18.
 35. Luongo JC, Fennelly KP, Keen JA, Zhai ZJ, Jones BW, Miller SL. Role of mechanical ventilation in the airborne transmission of infectious agents in buildings. *Indoor Air*. 2016;26:666–678.
 36. Allen JG, Ibrahim AM. Indoor air changes and potential implications for SARS-CoV-2 transmission. 2021:2.
 37. ASHRAE. Pandemic COVID-19 and Airborne Transmission: ASHRAE Environmental Health Committee Emerging Issue Brief. April 2020.
 38. Jones E, Young A, Clevenger K, et al. Risk Reduction Strategies for Reopening Schools. November 2020:60.
 39. Olsiewski PJ, Bruns R, Gronvall GK, et al. *School Ventilation: A Vital Tool to Reduce COVID-19 Spread*. Baltimore, MD: Johns Hopkins University Center for Health Security; 2021. May 2021. https://www.centerforhealthsecurity.org/our-work/pubs_archive/pubs-pdfs/2021/20210526-school-ventilation.pdf. Accessed June 1, 2021.
 40. REHVA. REHVA COVID-19 guidance document V4 -- How to operate HVAC and other building service systems to prevent the spread of the coronavirus(SARS-CoV-2) disease (COVID-19) in workplaces. November 2020.
 41. SAGE-EMG. Role of Ventilation in Controlling SARS-CoV-2 Transmission. September 2020. September 30, 2020. https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/928720/S0789_EMG_Role_of_Ventilation_in_Controlling_SARS-CoV-2_Transmission.pdf. Accessed April 2, 2021.
 42. WHO. Science in 5 - Episode #10 - Ventilation & COVID-19. October 2020. October 30, 2020. <https://www.who.int/emergencies/diseases/novel-coronavirus-2019/media-resources/science-in-5/episode-10---ventilation-covid-19>. Accessed April 2, 2021.
 43. WHO. *Roadmap to Improve and Ensure Good Indoor Ventilation in the Context of COVID-19*; 2021.
 44. Ferretti L, Ledda A, Wymant C, et al. The timing of COVID-19 transmission. *medRxiv*. September 2020:2020.09.04.20188516.
 45. Hasanoglu I, Korukluoglu G, Asilturk D, et al. Higher viral loads in asymptomatic COVID-19 patients might be the invisible part of the iceberg. *Infection*. 2021;49:117–126.
 46. He X, Lau EHY, Wu P, et al. Temporal dynamics in viral shedding and transmissibility of COVID-19. *Nat Med*. April 2020.

47. Johansson MA, Quandelacy TM, Kada S, et al. SARS-CoV-2 Transmission From People Without COVID-19 Symptoms. *JAMA Netw Open*. 2021;4:e2035057.
48. Yang Q, Saldi TK, Gonzales PK, et al. Just 2% of SARS-CoV-2–positive individuals carry 90% of the virus circulating in communities. *Proc Natl Acad Sci*. 2021;118. May 25, 2021. <https://www.pnas.org/content/118/21/e2104547118>. Accessed May 14, 2021.
49. Casey M, Griffin J, McAloon CG, et al. Pre-symptomatic transmission of SARS-CoV-2 infection: a secondary analysis using published data. *medRxiv*. June 2020:2020.05.08.20094870.
50. Gandhi M, Rutherford GW. Facial Masking for Covid-19 — Potential for “Variolation” as We Await a Vaccine. *N Engl J Med*. 2020;383:e101.
51. Beldomenico PM. Do superspreaders generate new superspreaders? A hypothesis to explain the propagation pattern of COVID-19. *Int J Infect Dis*. 2020;96:461–463.
52. Allen JG, MacNaughton P, Satish U, Santanam S, Vallarino J, Spengler JD. Associations of Cognitive Function Scores with Carbon Dioxide, Ventilation, and Volatile Organic Compound Exposures in Office Workers: A Controlled Exposure Study of Green and Conventional Office Environments. *Environ Health Perspect*. 2015.
53. Allen JG, Macomber JD. Healthy Buildings. April 21, 2020. <https://www.hup.harvard.edu/catalog.php?isbn=9780674237971>. Accessed May 27, 2021.
54. Fisk WJ. The ventilation problem in schools: literature review. *Indoor Air*. 2017;27:1039–1051.
55. Fisk WJ, Chan WR, Johnson AL. Does dampness and mold in schools affect health? Results of a meta-analysis. *Indoor Air*. 2019;29:895–902.
56. Sundell J, Levin H, Nazaroff WW, et al. Ventilation rates and health: multidisciplinary review of the scientific literature. *Indoor Air*. 2011;21:191–204.
57. Fisk WJ. Health benefits of particle filtration. *Indoor Air*. 2013;23:357–368.
58. IOM. *Clearing the Air: Asthma and Indoor Air Exposures*. Washington, D.C.: US Institute of Medicine Committee on the Assessment of Asthma and Indoor Air; 2000. January 19, 2000. <https://www.nap.edu/catalog/9610/clearing-the-air-asthma-and-indoor-air-exposures>. Accessed July 14, 2021.
59. McCormack MC, Breyse PN, Matsui EC, et al. Indoor particulate matter increases asthma morbidity in children with non-atopic and atopic asthma. *Ann Allergy Asthma Immunol*. 2011;106:308–315.
60. Berkowitz RL, Gao X, Michaels EK, Mujahid MS. Structurally vulnerable neighbourhood environments and racial/ethnic COVID-19 inequities. *Cities Health*. 2020;0:1–4.
61. Brandt EB, Beck AF, Mersha TB. Air pollution, racial disparities, and COVID-19 mortality. *J Allergy Clin Immunol*. 2020;146:61–63.

62. Dickinson KL, Roberts JD, Banacos N, et al. Structural Racism and the COVID-19 Experience in the United States. *Health Secur.* June 2021. June 1, 2021. <https://www.liebertpub.com/doi/10.1089/hs.2021.0031>. Accessed June 15, 2021.
63. Koh D. Migrant workers and COVID-19. *Occup Environ Med.* 2020;77:634–636.
64. Rozenfeld Y, Beam J, Maier H, et al. A model of disparities: risk factors associated with COVID-19 infection. *Int J Equity Health.* 2020;19:126.
65. Glover RE, van Schalkwyk MCI, Akl EA, et al. A framework for identifying and mitigating the equity harms of COVID-19 policy interventions. *J Clin Epidemiol.* 2020;128:35–48.
66. Prather KA, Marr LC, Schooley RT, McDiarmid MA, Wilson ME, Milton DK. Airborne transmission of SARS-CoV-2. *Science.* 2020;370:303–304.
67. Adenaiye OO, Lai J, Bueno de Mesquita PJ, et al. Infectious SARS-CoV-2 in Exhaled Aerosols and Efficacy of Masks During Early Mild Infection. *Clin Infect Dis.* 2021. September 14, 2021. <https://doi.org/10.1093/cid/ciab797>. Accessed September 15, 2021.
68. Chenari B, Dias Carrilho J, Gameiro da Silva M. Towards sustainable, energy-efficient and healthy ventilation strategies in buildings: A review. *Renew Sustain Energy Rev.* 2016;59:1426–1447.
69. Persily AK, Emmerich SJ. Indoor air quality in sustainable, energy efficient buildings. *HVACR Res.* 2012;18:4–20.
70. Melikov AK. Advanced air distribution: improving health and comfort while reducing energy use. *Indoor Air.* 2016;26:112–124.
71. Schiavon S, Melikov AK, Sekhar C. Energy analysis of the personalized ventilation system in hot and humid climates. *Energy Build.* 2010;42:699–707.
72. Seppänen OA. Ventilation Strategies for Good Indoor Air Quality and Energy Efficiency. *Int J Vent.* 2008;6:297–306.
73. Milton DK. A Rosetta Stone for Understanding Infectious Drops and Aerosols. *J Pediatr Infect Dis Soc.* 2020;9:413–415.
74. Prather KA, Marr LC, Schooley RT, McDiarmid MA, Wilson ME, Milton DK. Airborne transmission of SARS-CoV-2. *Science.* 2020;370:303–304.
75. Nazaroff WW. Indoor Aerosol Science Aspects of SARS-CoV-2 Transmission. July 2021. July 2, 2021. <https://escholarship.org/uc/item/14t2t7xs>. Accessed July 9, 2021.
76. Almstrand A-C, Bake B, Ljungström E, et al. Effect of airway opening on production of exhaled particles. *J Appl Physiol.* 2010;108:584–588.
77. Greening NJ, Larsson P, Ljungström E, Siddiqui S, Olin A-C. Small droplet emission in exhaled breath during different breathing manoeuvres: Implications for clinical lung function testing during COVID-19. *Allergy.* 2021;76:915–917.

78. Johnson GR, Morawska L, Ristovski ZD, et al. Modality of human expired aerosol size distributions. *J Aerosol Sci.* 2011;42:839–851.
79. Johnson GR, Morawska L. The Mechanism of Breath Aerosol Formation. *J Aerosol Med Pulm Drug Deliv.* 2009;22:229–237.
80. Morawska L, Buonanno G. The physics of particle formation and deposition during breathing. *Nat Rev Phys.* March 2021:1–2.
81. Pöhlker ML, Krüger OO, Förster J-D, et al. Respiratory aerosols and droplets in the transmission of infectious diseases. *ArXiv210301188 Phys.* April 2021. April 8, 2021. <http://arxiv.org/abs/2103.01188>. Accessed July 19, 2021.
82. Morawska L, Johnson GR, Ristovski ZD, et al. Size distribution and sites of origin of droplets expelled from the human respiratory tract during expiratory activities. *J Aerosol Sci.* 2009;40:256–269.
83. Asadi S, Wexler AS, Cappa CD, Barreda S, Bouvier NM, Ristenpart WD. Aerosol emission and superemission during human speech increase with voice loudness. *Sci Rep.* 2019;9.
84. Asadi S, Wexler AS, Cappa CD, Barreda S, Bouvier NM, Ristenpart WD. Effect of voicing and articulation manner on aerosol particle emission during human speech. *PLoS One.* 2020;15:e0227699.
85. Reid J. Comparing the Respirable Aerosol Concentrations and Particle Size Distributions Generated by Singing, Speaking and Breathing. August 2020.
86. Schijven J, Vermeulen LC, Swart A, Meijer A, Duizer E, de Roda Husman AM. Quantitative Microbial Risk Assessment for Airborne Transmission of SARS-CoV-2 via Breathing, Speaking, Singing, Coughing, and Sneezing. *Environ Health Perspect.* 2021;129:047002.
87. Bourouiba L, Dehandschoewercker E, Bush JWM. Violent expiratory events: on coughing and sneezing. *J Fluid Mech.* 2014;745:537–563.
88. Yan J, Grantham M, Pantelic J, et al. Infectious virus in exhaled breath of symptomatic seasonal influenza cases from a college community. *Proc Natl Acad Sci U S A.* 2018;115:1081–1086.
89. Aparna K, C. HX, Marisa H. Developing a Flexible National Wastewater Surveillance System for COVID-19 and Beyond. *Environ Health Perspect.* 2021;129:045002.
90. Peccia J, Zulli A, Brackney DE, et al. Measurement of SARS-CoV-2 RNA in wastewater tracks community infection dynamics. *Nat Biotechnol.* September 2020:1–4.
91. Ding Z, Qian H, Xu B, et al. Toilets dominate environmental detection of severe acute respiratory syndrome coronavirus 2 in a hospital. *Sci Total Environ.* 2021;753:141710.
92. Liu Y, Ning Z, Chen Y, et al. Aerodynamic Characteristics and RNA Concentration of SARS-CoV-2 Aerosol in Wuhan Hospitals during COVID-19 Outbreak. *bioRxiv.* 2020:2020.03.08.982637.

93. Li Y, Duan S, Yu ITS, Wong TW. Multi-zone modeling of probable SARS virus transmission by airflow between flats in Block E, Amoy Gardens. *Indoor Air*. 2005;15:96–111.
94. Yu ITS, Li Y, Wong TW, et al. Evidence of Airborne Transmission of the Severe Acute Respiratory Syndrome Virus. *N Engl J Med*. 2004;350:1731–1739.
95. Kang M, Wei J, Yuan J, et al. Probable Evidence of Fecal Aerosol Transmission of SARS-CoV-2 in a High-Rise Building. *Ann Intern Med*. 2020;173:974–980.
96. Morawska L. Droplet fate in indoor environments, or can we prevent the spread of infection? *Indoor Air*. 2006;16:335–347.
97. Fennelly KP. Particle sizes of infectious aerosols: implications for infection control. *Lancet Respir Med*. 2020;8:914–924.
98. Milton DK, Fabian MP, Cowling BJ, Grantham ML, McDevitt JJ. Influenza Virus Aerosols in Human Exhaled Breath: Particle Size, Culturability, and Effect of Surgical Masks. *PLOS Pathog*. 2013;9:e1003205.
99. Lindsley WG, Blachere FM, Thewlis RE, et al. Measurements of Airborne Influenza Virus in Aerosol Particles from Human Coughs. *PLoS ONE*. 2010;5. November 30, 2010. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2994911/>. Accessed March 29, 2021.
100. Coleman KK, Tay DJW, Tan KS, et al. Viral Load of Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) in Respiratory Aerosols Emitted by Patients With Coronavirus Disease 2019 (COVID-19) While Breathing, Talking, and Singing. *Clin Infect Dis*. 2021. August 6, 2021. <https://doi.org/10.1093/cid/ciab691>. Accessed October 7, 2021.
101. Marr LC, Tang JW, Van Mullekom J, Lakdawala SS. Mechanistic insights into the effect of humidity on airborne influenza virus survival, transmission and incidence. *J R Soc Interface*. 2019;16:20180298.
102. NASEM. *Airborne Transmission of SARS-CoV-2: Proceedings of a Workshop—in Brief*; 2020. October 2020. <https://www.nap.edu/read/25958/chapter/1>. Accessed April 16, 2021.
103. Wells WF. On air-borne infection study II. Droplets and droplet nuclei. *Am J Epidemiol*. 1934;20:611–618.
104. Xie X, Li Y, Chwang AT, Ho PL, Seto WH. How far droplets can move in indoor environments--revisiting the Wells evaporation-falling curve. *Indoor Air*. 2007;17:211–25.
105. Mao N, An CK, Guo LY, et al. Transmission risk of infectious droplets in physical spreading process at different times: A review. *Build Environ*. 2020;185:107307.
106. Netz RR. Mechanisms of Airborne Infection via Evaporating and Sedimenting Droplets Produced by Speaking. *J Phys Chem B*. 2020;124:7093–7101.
107. Abkarian M, Mendez S, Xue N, Yang F, Stone HA. Speech can produce jet-like transport relevant to asymptomatic spreading of virus. *Proc Natl Acad Sci*. 2020;117:25237–25245.

108. Bourouiba L. Fluid Dynamics of Respiratory Infectious Diseases. *Annu Rev Biomed Eng.* 2021;23:547–577.
109. Mittal R, Ni R, Seo J-H. The flow physics of COVID-19. *J Fluid Mech.* 2020;894. July 2020. <https://www.cambridge.org/core/journals/journal-of-fluid-mechanics/article/flow-physics-of-covid19/476E32549012B3620D2452F30F2567F1>. Accessed August 12, 2021.
110. Ai ZT, Melikov AK. Airborne spread of expiratory droplet nuclei between the occupants of indoor environments: A review. *Indoor Air.* 2018;28:500–524.
111. Chen W, Zhang N, Wei J, Yen H-L, Li Y. Short-range airborne route dominates exposure of respiratory infection during close contact. *Build Environ.* 2020;176:106859.
112. Baron PA. Factors Affecting Aerosol Sampling. *NIOSH Man Anal Methods NMAM 5th Ed.* 2016:35.
113. Hinds WC. *Aerosol Technology: Properties, Behavior, and Measurement of Airborne Particles.* 2nd ed. New York: Wiley; 1999.
114. Nardell EA. Transmission and institutional infection control of tuberculosis. *Cold Spring Harb Perspect Med.* 2016;6. February 2016. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4743075/>. Accessed April 15, 2021.
115. Tellier R, Li Y, Cowling BJ, Tang JW. Recognition of aerosol transmission of infectious agents: a commentary. *BMC Infect Dis.* 2019;19:101.
116. Hou YJ, Okuda K, Edwards CE, et al. SARS-CoV-2 Reverse Genetics Reveals a Variable Infection Gradient in the Respiratory Tract. *Cell.* 2020;182:429-446.e14.
117. Bixler SL, Stefan CP, Jay A, et al. Aerosol Exposure of Cynomolgus Macaques to SARS-CoV-2 Results in More Severe Pathology than Existing Models. *bioRxiv.* April 2021:2021.04.27.441510.
118. Lednicky JA, Loeb JC. Detection and Isolation of Airborne Influenza A H3N2 Virus Using a Sioutas Personal Cascade Impactor Sampler. *Influenza Res Treat.* 2013;2013.
119. Lednicky JA, Shankar SN, Elbadry MA, et al. Collection of SARS-CoV-2 Virus from the Air of a Clinic within a University Student Health Care Center and Analyses of the Viral Genomic Sequence. *Aerosol Air Qual Res.* 2020;20:1167–1171.
120. Chia PY, Coleman KK, Tan YK, et al. Detection of air and surface contamination by SARS-CoV-2 in hospital rooms of infected patients. *Nat Commun.* 2020;11:2800.
121. Leung NHL, Zhou J, Chu DKW, et al. Quantification of influenza virus RNA in aerosols in patient rooms. *PLOS ONE.* 2016;11:e0148669.
122. Yang W, Elankumaran S, Marr LC. Concentrations and size distributions of airborne influenza A viruses measured indoors at a health centre, a day-care centre and on aeroplanes. *J R Soc Interface.* 2011;8:1176–1184.

123. Yadana S, Coleman KK, Nguyen TT, et al. Monitoring for airborne respiratory viruses in a general pediatric ward in Singapore. *J Public Health Res.* 2019;8. December 4, 2019. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6902309/>. Accessed June 2, 2021.
124. Blachere FM, Lindsley WG, Pearce TA, et al. Measurement of Airborne Influenza Virus in a Hospital Emergency Department. *Clin Infect Dis.* 2009;48:438–440.
125. Coleman KK, Nguyen TT, Yadana S, Hansen-Estruch C, Lindsley WG, Gray GC. Bioaerosol Sampling for Respiratory Viruses in Singapore’s Mass Rapid Transit Network. *Sci Rep.* 2018;8:17476.
126. Coleman KK, Sigler WV. Airborne Influenza A Virus Exposure in an Elementary School. *Sci Rep.* 2020;10:1859.
127. Riley RL, O’Grady FCN-R. RQW 700 R 1961 614. 4. *Airborne Infection: Transmission and Control.* New York,: Macmillan; 1961.
128. Harper GJ. Airborne micro-organisms: survival tests with four viruses. *J Hyg Lond.* 1961;59:479–86.
129. Schuit M, Ratnesar-Shumate S, Yolitz J, et al. Airborne SARS-CoV-2 is Rapidly Inactivated by Simulated Sunlight. *J Infect Dis.* June 2020. June 11, 2020. <http://academic.oup.com/jid/advance-article/doi/10.1093/infdis/jiaa334/5856149>.
130. van Doremalen N, Bushmaker T, Morris DH, et al. Aerosol and surface stability of SARS-CoV-2 as compared with SARS-CoV-1. *N Engl J Med.* 2020;382:1564–1567.
131. Pineda Rojas AL, Cordo SM, Saurral RI, Jimenez JL, Marr LC, Kropff E. Relative Humidity Predicts Day-to-Day Variations in COVID-19 Cases in the City of Buenos Aires. *Environ Sci Technol.* July 2021:acs.est.1c02711.
132. Beggs CB, Avital EJ. A psychrometric model to assess the biological decay of the SARS-CoV-2 virus in aerosols. *PeerJ.* 2021;9. March 2, 2021. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7934646/>. Accessed May 21, 2021.
133. Morris DH, Yinda KC, Gamble A, et al. The effect of temperature and humidity on the stability of SARS-CoV-2 and other enveloped viruses. *BioRxiv Prepr Serv Biol.* October 2020.
134. Tang JW. The effect of environmental parameters on the survival of airborne infectious agents. *J R Soc Interface.* 2009;6:S737–S746.
135. Kormuth KA, Lin K, Prussin AJ II, et al. Influenza virus infectivity is retained in aerosols and droplets independent of relative humidity. *J Infect Dis.* 2018;218:739–747.
136. Lin K, Marr LC. Humidity-dependent decay of viruses, but not bacteria, in aerosols and droplets follows disinfection kinetics. *Environ Sci Technol.* 2020;54:1024–1032.
137. Dabisch P, Schuit M, Herzog A, et al. The influence of temperature, humidity, and simulated sunlight on the infectivity of SARS-CoV-2 in aerosols. *Aerosol Sci Technol.* 2021;55:142–153.

138. Kudo E, Song E, Yockey LJ, et al. Low ambient humidity impairs barrier function and innate resistance against influenza infection. *Proc Natl Acad Sci*. 2019;116:10905–10910.
139. IOM. *Human Health Effects Associated with Damp Indoor Environments*. Vol US Institute of Medicine Committee on Damp Indoor Spaces and Health. Washington D.C: National Academies Press (US); 2004. 2004. <https://www.ncbi.nlm.nih.gov/books/NBK215639/>. Accessed July 1, 2021.
140. Li Y. The respiratory infection inhalation route continuum. *Indoor Air*. 2021;31:279–281.
141. Ng OT, Marimuthu K, Koh V, et al. SARS-CoV-2 seroprevalence and transmission risk factors among high-risk close contacts: a retrospective cohort study. *Lancet Infect Dis*. 2021;21:333–343.
142. Zhang N, Chen W, Chan P-T, Yen H-L, Tang JW-T, Li Y. Close contact behavior in indoor environment and transmission of respiratory infection. *Indoor Air*. 2020;30:645–661.
143. Tang JW, Marr LC, Milton DK. Aerosols should not be defined by distance travelled. *J Hosp Infect*. 2021;0. May 25, 2021. [https://www.journalofhospitalinfection.com/article/S0195-6701\(21\)00210-3/abstract](https://www.journalofhospitalinfection.com/article/S0195-6701(21)00210-3/abstract). Accessed June 10, 2021.
144. CDC. Contact Tracing for COVID-19. Centers for Disease Control and Prevention. February 25, 2021. <https://www.cdc.gov/coronavirus/2019-ncov/php/contact-tracing/contact-tracing-plan/contact-tracing.html>. Accessed July 7, 2021.
145. Gao CX, Li Y, Wei J, et al. Multi-route respiratory infection: When a transmission route may dominate. *Sci Total Environ*. 2021;752:141856.
146. Kwon K-S, Park J-I, Park YJ, Jung D-M, Ryu K-W, Lee J-H. Evidence of Long-Distance Droplet Transmission of SARS-CoV-2 by Direct Air Flow in a Restaurant in Korea. *J Korean Med Sci*. 2020;35. November 23, 2020. <https://doi.org/10.3346/jkms.2020.35.e415>. Accessed May 17, 2021.
147. Stein-Zamir C, Abramson N, Shoob H, et al. A large COVID-19 outbreak in a high school 10 days after schools' reopening, Israel, May 2020. *Eurosurveillance*. 2020;25:2001352.
148. Herstein JJ, Degarege A, Stover D, et al. Characteristics of SARS-CoV-2 transmission among meat processing workers in Nebraska, USA, and effectiveness of risk mitigation measures. *Emerg Infect Dis*. 2021;27:1032–1038.
149. Chaw L, Koh WC, Jamaludin SA, Naing L, Alikhan MF, Wong J. Analysis of SARS-CoV-2 Transmission in Different Settings, Brunei - Volume 26, Number 11—November 2020 - Emerging Infectious Diseases journal - CDC. November 2020. November 2020. https://wwwnc.cdc.gov/eid/article/26/11/20-2263_article. Accessed May 17, 2021.
150. Katelaris AL, Wells J, Clark P, et al. Epidemiologic evidence for airborne transmission of SARS-CoV-2 during church singing, Australia, 2020. *Emerg Infect Dis*. 2021;27. April 5, 2021. https://wwwnc.cdc.gov/eid/article/27/6/21-0465_article.
151. Wong NS, Lee SS, Kwan TH, Yeoh E-K. Settings of virus exposure and their implications in the propagation of transmission networks in a COVID-19 outbreak. *Lancet Reg Health – West Pac*. 2020;4. November 1, 2020. [https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065\(20\)30052-3/abstract](https://www.thelancet.com/journals/lanwpc/article/PIIS2666-6065(20)30052-3/abstract). Accessed May 17, 2021.

152. Edwards NJ, Widrick R, Wilmes J, et al. Reducing COVID-19 airborne transmission risks on public transportation buses: an empirical study on aerosol dispersion and control. *medRxiv*. March 2021;2021.02.25.21252220.
153. Shen Y, Li C, Dong H, et al. Community Outbreak Investigation of SARS-CoV-2 Transmission Among Bus Riders in Eastern China. *JAMA Intern Med*. September 2020.
154. de Man P, Paltansing S, Ong DSY, Vaessen N, van Nielen G, Koeleman JGM. Outbreak of COVID-19 in a nursing home associated with aerosol transmission as a result of inadequate ventilation. *Clin Infect Dis Off Publ Infect Dis Soc Am*. 2020;73:170–171.
155. Chu DKW, Gu H, Chang LDJ, et al. SARS-CoV-2 Superspread in Fitness Center, Hong Kong, China, March 2021 -. *Emerg Infect Dis*. 2021;27. August 2021.
https://wwwnc.cdc.gov/eid/article/27/8/21-0833_article. Accessed June 23, 2021.
156. Dougherty K, Mannell M, Naqvi O, Matson D, Stone J. SARS-CoV-2 B.1.617.2 (Delta) Variant COVID-19 Outbreak Associated with a Gymnastics Facility — Oklahoma, April–May 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70. July 9, 2021.
http://www.cdc.gov/mmwr/volumes/70/wr/mm7028e2.htm?s_cid=mm7028e2_w. Accessed July 12, 2021.
157. Groves LM. Community Transmission of SARS-CoV-2 at Three Fitness Facilities — Hawaii, June–July 2020. *MMWR Morb Mortal Wkly Rep*. 2021;70. 2021.
<https://www.cdc.gov/mmwr/volumes/70/wr/mm7009e1.htm>. Accessed June 15, 2021.
158. Jang S, Han SH, Rhee J-Y. Cluster of coronavirus disease associated with fitness dance classes, South Korea. *Emerg Infect Dis*. 2020;26:1917–1920.
159. Lendacki FR. COVID-19 Outbreak Among Attendees of an Exercise Facility — Chicago, Illinois, August–September 2020. *MMWR Morb Mortal Wkly Rep*. 2021;70. 2021.
<https://www.cdc.gov/mmwr/volumes/70/wr/mm7009e2.htm>. Accessed June 23, 2021.
160. Chandrasekhar R, Sloan C, Mitchel E, et al. Social determinants of influenza hospitalization in the United States. *Influenza Other Respir Viruses*. 2017;11:479–488.
161. Madewell ZJ, Yang Y, Longini IM, Halloran ME, Dean NE. Household transmission of SARS-CoV-2: A systematic review and meta-analysis. *JAMA Netw Open*. 2020;3:e2031756.
162. Ge X-Y, Pu Y, Liao C-H, et al. Evaluation of the exposure risk of SARS-CoV-2 in different hospital environment. *Sustain Cities Soc*. 2020;61:102413.
163. Richterman A, Meyerowitz EA, Cevik M. Hospital-Acquired SARS-CoV-2 Infection: Lessons for Public Health. *JAMA*. 2020;324:2155.
164. Cheng VC-C, Wong S-C, Yuen K-Y. Estimating Coronavirus Disease 2019 Infection Risk in Health Care Workers. *JAMA Netw Open*. 2020;3:e209687.
165. Chu DK, Akl EA, Duda S, et al. Physical distancing, face masks, and eye protection to prevent person-to-person transmission of SARS-CoV-2 and COVID-19: a systematic review and meta-analysis. *Lancet Lond Engl*. 2020;395:1973–1987.

166. Goldberg L, Levinsky Y, Marcus N, et al. SARS-CoV-2 Infection Among Health Care Workers Despite the Use of Surgical Masks and Physical Distancing—the Role of Airborne Transmission. *Open Forum Infect Dis.* 2021;8. March 1, 2021. <https://doi.org/10.1093/ofid/ofab036>. Accessed March 26, 2021.
167. Klompas M, Baker MA, Griesbach D, et al. Transmission of SARS-CoV-2 from asymptomatic and presymptomatic individuals in healthcare settings despite medical masks and eye protection. *Clin Infect Dis.* March 2021.
168. Nguyen LH, Drew DA, Graham MS, et al. Risk of COVID-19 among front-line health-care workers and the general community: a prospective cohort study. *Lancet Public Health.* 2020;5:e475–e483.
169. Qiu X, Miller JC, MacFadden DR, Hanage WP. Evaluating the contributions of strategies to prevent SARS-CoV-2 transmission in the healthcare setting: a modelling study. *BMJ Open.* 2021;11:e044644.
170. VoPham T, Weaver MD, Adamkiewicz G, Hart JE. Social Distancing Associations with COVID-19 Infection and Mortality Are Modified by Crowding and Socioeconomic Status. *Int J Environ Res Public Health.* 2021;18:4680.
171. Riley EC, Murphy G, Riley RL. Airborne spread of measles in a suburban elementary school. *Am J Epidemiol.* 1978;107:421–432.
172. Wells WF. *Airborne Contagion and Air Hygiene: An Ecological Study of Droplet Infection.* Cambridge, MA: Harvard University Press; 1955.
173. Rudnick SN, Milton DK. Risk of indoor airborne infection transmission estimated from carbon dioxide concentration. *Indoor Air.* 2003;13:237–245.
174. Bueno de Mesquita PJ, Noakes CJ, Milton DK. Quantitative aerobiologic analysis of an influenza human challenge-transmission trial. *Indoor Air.* 2020;30:1189–1198.
175. Nardell EA. Indoor environmental control of tuberculosis and other airborne infections. *Indoor Air.* 2016;26:79–87.
176. Bond TC, Bosco-Lauth A, Farmer DK, et al. Quantifying Proximity, Confinement, and Interventions in Disease Outbreaks: A Decision Support Framework for Air-Transported Pathogens. *Environ Sci Technol.* 2021;55:2890–2898.
177. Chao CYH, Wan MP, Morawska L, et al. Characterization of expiration air jets and droplet size distributions immediately at the mouth opening. *J Aerosol Sci.* 2009;40:122–133.
178. Lindsley WG, Beezhold DH, Coyle J, et al. Efficacy of universal masking for source control and personal protection from simulated cough and exhaled aerosols in a room. *medRxiv.* April 2021:2021.04.21.21258880.
179. Pan J, Harb C, Leng W, Marr LC. Inward and outward effectiveness of cloth masks, a surgical mask, and a face shield. *Aerosol Sci Technol.* 2021;55:718–733.

180. UK SAGE. *EMG: Role of Screens and Barriers in Mitigating COVID-19 Transmission, 1 July 2021*. UK Scientific Advisory Group for Emergencies Environmental Modelling Group (EMG); 2021. July 1, 2021. <https://www.gov.uk/government/publications/emg-role-of-screens-and-barriers-in-mitigating-covid-19-transmission-1-july-2021>. Accessed August 2, 2021.
181. Gilkeson CA, Camargo-Valero MA, Pickin LE, Noakes CJ. Measurement of ventilation and airborne infection risk in large naturally ventilated hospital wards. *Build Environ*. 2013;65:35–48.
182. Noakes CJ, Sleigh PA, Escombe AR, Beggs CB. Use of CFD Analysis in Modifying a TB Ward in Lima, Peru. *Indoor Built Environ*. 2006;15:41–47.
183. Epple P, Steppert M, Florschütz M, Dahlem P. Partition walls as effective protection from bio-aerosols in classrooms – an experimental investigation. *GMS Hyg Infect Control*. 2021;16:Doc09.
184. Ishigaki Y, Kawauchi Y, Yokogawa S, Saito A, Kitamura H, Moritake T. Experimental investigation to verify if excessive plastic sheeting shielding produce micro clusters of SARS-CoV-2. *medRxiv*. May 2021:2021.05.22.21257321.
185. Lessler J, Grabowski MK, Grantz KH, et al. Household COVID-19 risk and in-person schooling. *Science*. April 2021. April 29, 2021. <https://science.sciencemag.org/content/early/2021/04/28/science.abh2939>.
186. Pichurov G, Srebric J, Zhu S, Vincent RL, Brickner PW, Rudnick SN. A validated numerical investigation of the ceiling fan’s role in the upper-room UVGI efficacy. *Build Environ*. 2015;86:109–119.
187. Darouiche RO, Green DM, Harrington MA, et al. Association of Airborne Microorganisms in the Operating Room With Implant Infections: A Randomized Controlled Trial. *Infect Control Hosp Epidemiol*. 2017;38:3–10.
188. Dungi SR, Ghia U, Mead KR, Gressel M. Effectiveness of a Local Ventilation/Filtration Intervention for Health-Care Worker Exposure Reduction to Airborne Infection in a Hospital Room. *ASHRAE Trans*. 2015;121:1Q,2Q,3Q,4Q,5Q,6Q,7Q,8Q.
189. Küpper M, Asbach C, Schneiderwind U, Finger H, Spiegelhoff D, Schumacher S. Testing of an Indoor Air Cleaner for Particulate Pollutants under Realistic Conditions in an Office Room. *Aerosol Air Qual Res*. 2019;19:1655–1665.
190. Lindsley WG, Derk RC, Coyle JP, et al. Efficacy of Portable Air Cleaners and Masking for Reducing Indoor Exposure to Simulated Exhaled SARS-CoV-2 Aerosols — United States, 202. *Morb Mortal Wkly Rep MMWR*. 2021;70:5.
191. Hamner L. High SARS-CoV-2 Attack Rate Following Exposure at a Choir Practice — Skagit County, Washington, March 2020. *MMWR Morb Mortal Wkly Rep*. 2020;69. May 12, 2020. <https://www.cdc.gov/mmwr/volumes/69/wr/mm6919e6.htm>. Accessed May 13, 2020.
192. Kriegel M, Buchholz U, Gastmeier P, Bischoff P, Abdelgawad I, Hartmann A. Predicted Infection Risk for Aerosol Transmission of SARS-CoV-2. *medRxiv*. November 2020:2020.10.08.20209106.

193. van den Berg P, Schechter-Perkins EM, Jack RS, et al. Effectiveness of three versus six feet of physical distancing for controlling spread of COVID-19 among primary and secondary students and staff: A retrospective, state-wide cohort study. *Clin Infect Dis*. March 2021:ciab230.
194. Mousavi ES, Grosskopf KR. Directional Airflow and Ventilation in Hospitals: A Case Study of Secondary Airborne Infection. *Energy Procedia*. 2015;78:1201–1206.
195. Cameron JL. Early Contributions to the Johns Hopkins Hospital by the “Other” Surgeon: John Shaw Billings. *Ann Surg*. 2001;234:267–278.
196. Iddon C. Florence Nightingale: nurse and building engineer. *CIBSE J*. May 2015. May 2015. <https://www.cibsejournal.com/general/florence-nightingale-nurse-and-building-engineer/>. Accessed March 30, 2021.
197. Du C-R, Wang S-C, Yu M-C, et al. Effect of ventilation improvement during a tuberculosis outbreak in underventilated university buildings. *Indoor Air*. 2020;30:422–432.
198. Gao X, Li Y, Xu P, Cowling BJ. Evaluation of intervention strategies in schools including ventilation for influenza transmission control. *Build Simul*. 2012;5:29–37.
199. Gao X, Wei J, Cowling BJ, Li Y. Potential impact of a ventilation intervention for influenza in the context of a dense indoor contact network in Hong Kong. *Sci Total Environ*. 2016;569–570:373–381.
200. Gao X, Wei J, Lei H, Xu P, Cowling BJ, Li Y. Building Ventilation as an Effective Disease Intervention Strategy in a Dense Indoor Contact Network in an Ideal City. *PLOS ONE*. 2016;11:e0162481.
201. Jones B, Sharpe P, Iddon C, Hathway EA, Noakes CJ, Fitzgerald S. Modelling uncertainty in the relative risk of exposure to the SARS-CoV-2 virus by airborne aerosol transmission in well mixed indoor air. *Build Environ*. 2021;191:107617.
202. Menzies D, Fanning A, Yuan L, Mark Fitzgerald J. Hospital Ventilation and Risk for Tuberculous Infection in Canadian Health Care Workers. *Ann Intern Med*. November 2000. November 21, 2000. <https://www.acpjournals.org/doi/abs/10.7326/0003-4819-133-10-200011210-00010>. Accessed March 26, 2021.
203. Zhu S, Jenkins S, Addo K, et al. Ventilation and laboratory confirmed acute respiratory infection (ARI) rates in college residence halls in College Park, Maryland. *Environ Int*. 2020;137:105537.
204. Qian H, Zheng X. Ventilation control for airborne transmission of human exhaled bio-aerosols in buildings. *J Thorac Dis*. 2018;10. July 2018. <https://jtd.amegroups.com/article/view/18723>. Accessed March 26, 2021.
205. Miller SL, Nazaroff WW, Jimenez JL, et al. Transmission of SARS-CoV-2 by inhalation of respiratory aerosol in the Skagit Valley Chorale superspreading event. *Indoor Air*. 2020;31:314–323.
206. Moser MR, Bender TR, Margolis HS, Noble GR, Kendal AP, Ritter DG. An outbreak of influenza aboard a commercial airliner. *Am J Epidemiol*. 1979;110:1–6.

207. Shen Y, Xu W, Li C, et al. A Cluster of Novel Coronavirus Disease 2019 Infections Indicating Person-to-Person Transmission Among Casual Contacts From Social Gatherings: An Outbreak Case-Contact Investigation. *Open Forum Infect Dis*. 2020;7:ofaa231.
208. Bazant MZ, Bush JWM. A guideline to limit indoor airborne transmission of COVID-19. *Proc Natl Acad Sci*. 2021;118. April 27, 2021. <https://www.pnas.org/content/118/17/e2018995118>. Accessed May 21, 2021.
209. Melikov AK, Ai ZT, Markov DG. Intermittent occupancy combined with ventilation: An efficient strategy for the reduction of airborne transmission indoors. *Sci Total Environ*. 2020;744:140908.
210. Zhang S, Ai Z, Lin Z. Occupancy-aided ventilation for both airborne infection risk control and work productivity. *Build Environ*. 2021;188:107506.
211. Nguyen-Van-Tam JS, Killingley B, Enstone J, et al. Minimal transmission in an influenza A (H3N2) human challenge-transmission model within a controlled exposure environment. *PLoS Pathog*. 2020;16:e1008704.
212. ASHRAE. Standard 170-2021 - Ventilation of Health Care Facilities. 2021. 2021. https://ashrae.iwrapper.com/ASHRAE_PREVIEW_ONLY_STANDARDS/STD_170_2021. Accessed April 2, 2021.
213. Atkinson J, Chartier Y, Pessoa-Silva CL, Jensen P, Li Y, Seto W-H. *Articles Included in the Systematic Review on the Association between Ventilation and Infection*. World Health Organization; 2009. 2009. <http://www.ncbi.nlm.nih.gov/books/NBK143276/>. Accessed March 26, 2021.
214. WHO. *Infection Prevention and Control during Health Care When COVID-19 Is Suspected: Interim Guidance*. World Health Organization; 2020. March 19, 2020. <https://apps.who.int/iris/bitstream/handle/10665/331495/WHO-2019-nCoV-IPC-2020.3-eng.pdf?sequence=1&isAllowed=y>. Accessed June 23, 2021.
215. Escombe AR, Ticona E, Chávez-Pérez V, Espinoza M, Moore DAJ. Improving natural ventilation in hospital waiting and consulting rooms to reduce nosocomial tuberculosis transmission risk in a low resource setting. *BMC Infect Dis*. 2019;19.
216. Chan WR, Li X, Singer BC, et al. Ventilation rates in California classrooms: Why many recent HVAC retrofits are not delivering sufficient ventilation. *Build Environ*. 2020;167:106426.
217. Mendell MJ, Eliseeva EA, Davies MM, et al. Association of classroom ventilation with reduced illness absence: a prospective study in California elementary schools. *Indoor Air*. 2013;23:515–528.
218. Azimi P, Stephens B. HVAC filtration for controlling infectious airborne disease transmission in indoor environments: Predicting risk reductions and operational costs. *Build Environ*. 2013;70:150–160.
219. Kohanski MA, Lo LJ, Waring MS. Review of indoor aerosol generation, transport, and control in the context of COVID-19. *Int Forum Allergy Rhinol*. 2020;10:1173–1179.
220. ASHRAE. ASHRAE Position Document on Infectious Aerosols. April 2020.

221. Zaatari M, Novoselac A, Siegel J. The relationship between filter pressure drop, indoor air quality, and energy consumption in rooftop HVAC units. *Build Environ*. 2014;73:151–161.
222. Mousavi ES, Kananizadeh N, Martinello RA, Sherman JD. COVID-19 outbreak and hospital air quality: A systematic review of evidence on air filtration and recirculation. *Environ Sci Technol*. 2021;55:4134–4147.
223. Zhang J, Huntley D, Fox A, GERHARDT B, Vatine A, Cherne J. Study of Viral Filtration Performance of Residential HVAC Filters. *ASHRAE J*. August 2020.
224. ASHRAE. *Standard 52.2-1999. Method of Testing General Ventilation Air-Cleaning Devices for Removal Efficiency by Particle Size*. Atlanta, GA; 1999.
225. Stephens B. HVAC filtration and the Wells-Riley approach to assessing risks of infectious airborne diseases. *Natl Air Filtr Assoc NAFA Found Rep*. 2012.
226. Curtius J, Granzin M, Schrod J. Testing mobile air purifiers in a school classroom: Reducing the airborne transmission risk for SARS-CoV-2. *Aerosol Sci Technol*. 2021;0:1–14.
227. ASHRAE. *In-Room Air Cleaner Guidance for Reducing COVID-19 in Air in Your Space/Room*. American Society of Heating, Refrigerating and Air-Conditioning Engineers; 2021. January 21, 2021. <https://www.ashrae.org/file%20library/technical%20resources/covid-19/in-room-air-cleaner-guidance-for-reducing-covid-19-in-air-in-your-space-or-room.pdf>. Accessed August 6, 2021.
228. Rosenthal J. A Variation on the “Box Fan with MERV 13 Filter” Air Cleaner. *Tex-Air Filters*. August 2020. August 22, 2020. <https://www.texairfilters.com/a-variation-on-the-box-fan-with-merv-13-filter-air-cleaner/>. Accessed July 13, 2021.
229. Beggs CB, Avital EJ. Upper-room ultraviolet air disinfection might help to reduce COVID-19 transmission in buildings: a feasibility study. *PeerJ*. 2020;8. October 13, 2020. <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7566754/>. Accessed March 26, 2021.
230. Kowalski W. *Ultraviolet Germicidal Irradiation Handbook: UVGI for Air and Surface Disinfection*. Berlin, Heidelberg: Springer; 2009. 2009. <https://doi.org/10.1007/978-3-642-01999-9>.
231. Reed NG. The History of Ultraviolet Germicidal Irradiation for Air Disinfection. *Public Health Rep*. 2010;125:15–27.
232. Riley RL, Mills CC, O’grady F, Sultan LU, Wittstadt F, Shivpuri DN. Infectiousness of air from a tuberculosis ward. Ultraviolet irradiation of infected air: comparative infectiousness of different patients. *Am Rev Respir Dis*. 1962;85:511–525.
233. Walker CM, Ko G. Effect of ultraviolet germicidal irradiation on viral aerosols. *Environ Sci Technol*. 2007;41:5460–5.
234. Wells WF, Wells MW, Wilder TS. The environmental control of epidemic contagion I. An epidemiologic study of radiant disinfection of air in day schools. *Am J Epidemiol*. 1942;35:97–121.

235. Miller S, Hernandez M, Fennelly K, et al. *Efficacy of Ultraviolet Irradiation in Controlling the Spread of Tuberculosis; Submitted to: Centers for Disease Control and Prevention National Institute for Occupational Safety and Health.*; 2002. October 19, 2002.
<https://stacks.cdc.gov/view/cdc/11285>. Accessed July 26, 2021.
236. First MW, Weker RA, Yasui S, Nardell EA. Monitoring human exposures to upper-room germicidal ultraviolet irradiation. *J Occup Environ Hyg.* 2005;2:285–292.
237. Juarez-Leon FA, Soriano-Sánchez AG, Rodríguez-Licea MA, Perez-Pinal FJ. Design and Implementation of a Germicidal UVC-LED Lamp. *IEEE Access.* 2020;8:196951–196962.
238. IES Photobiology Committee. *IES Committee Report: Germicidal Ultraviolet (GUV) – Frequently Asked Questions.* USA: Illuminating Engineering Society; 2020. May 5, 2020.
<https://media.ies.org/docs/standards/IES%20CR-2-20-V1a-20200507.pdf>. Accessed August 6, 2021.
239. Nardell EA, Bucher SJ, Brickner PW, et al. Safety of Upper-Room Ultraviolet Germicidal Air Disinfection for Room Occupants: Results from the Tuberculosis Ultraviolet Shelter Study. *Public Health Rep.* 2008;123:52–60.
240. Brantner C, Wong A, Davis A, Hammond C, Olson N. *Safety of 222 Nm Band-Pass Filtered Irradiation: A Review and Analysis of Current Data.* Boeing; 2020:12.
241. Buonanno M, Ponnaiya B, Welch D, et al. Germicidal efficacy and mammalian skin safety of 222-nm UV light. *Radiat Res.* 2017;187:483–491.
242. Gao X, Li Y, Leung GM. Ventilation Control of Indoor Transmission of Airborne Diseases in an Urban Community. *Indoor Built Environ.* 2009;18:205–218.
243. McDevitt JJ, Milton DK, Rudnick SN, First MW. Inactivation of poxviruses by upper-room UVC light in a simulated hospital room environment. *PloS One.* 2008;3:e3186.
244. McDevitt JJ, Rudnick SN, Radonovich LJ. Aerosol susceptibility of influenza virus to UV-C light. *Appl Environ Microbiol.* 2012;78:1666–1669.
245. Peccia J, Werth HM, Miller S, Hernandez M. Effects of Relative Humidity on the Ultraviolet Induced Inactivation of Airborne Bacteria. *Aerosol Sci Technol.* 2001;35:728–740.
246. Zhu S, Srebric J, Rudnick SN, Vincent RL, Nardell EA. Numerical Modeling of Indoor Environment with a Ceiling Fan and an Upper-Room Ultraviolet Germicidal Irradiation System. *Build Environ.* 2014;72:116–124.
247. Riley RL, Nardell EA. Clearing the air. The theory and application of ultraviolet air disinfection. *Am Rev Respir Dis.* 1989;139:1286–1294.
248. Xu P, Peccia J, Fabian P, et al. Efficacy of ultraviolet germicidal irradiation of upper-room air in inactivating airborne bacterial spores and mycobacteria in full-scale studies. *Atmos Environ.* 2003;37:405–419.
249. Ko G, First MW, Burge HA. The characterization of upper-room ultraviolet germicidal irradiation in inactivating airborne microorganisms. *Environ Health Perspect.* 2002;110:95–101.

250. Wells WF. Air Disinfection in Day Schools. *Am J Public Health Nations Health*. 1943;33:1436–1443.
251. Riley RL. Airborne infection. *Am J Med*. 1974;57:466–475.
252. Wengraitis S, Reed NG. Ultraviolet spectral reflectance of ceiling tiles, and implications for the safe use of upper-room ultraviolet germicidal irradiation. *Photochem Photobiol*. 2012;88:1480–1488.
253. Lee B, Bahnfleth WP. Effects of installation location on performance and economics of in-duct ultraviolet germicidal irradiation systems for air disinfection. *Build Environ*. 2013;67:193–201.
254. Menzies D, Popa J, Hanley JA, Rand T, Milton DK. Effect of ultraviolet germicidal lights installed in office ventilation systems on workers' health and wellbeing: double-blind multiple crossover trial. *Lancet*. 2003;362:1785–91.
255. Bahnfleth WP. Cooling coil ultraviolet germicidal irradiation. *ASHRAE J*. 2017;59:72–74.
256. Firrantello J, Bahnfleth W. Simulation and monetization of collateral airborne infection risk improvements from ultraviolet germicidal irradiation for coil maintenance. *Sci Technol Built Environ*. 2018;24:135–148.
257. Firrantello J, Bahnfleth W. Field measurement and modeling of UVC cooling coil irradiation for heating, ventilating, and air conditioning energy use reduction (RP-1738)—Part 2: Energy, indoor air quality, and economic modeling. *Sci Technol Built Environ*. 2018;24:600–611.
258. Wang Y, Sekhar C, Bahnfleth WP, Cheong KW, Firrantello J. Effectiveness of an ultraviolet germicidal irradiation system in enhancing cooling coil energy performance in a hot and humid climate. *Energy Build*. 2016;130:321–329.
259. Wang Y, Sekhar C, Bahnfleth WP, Cheong KW, Firrantello J. Effects of an ultraviolet coil irradiation system on the airside heat transfer coefficient and low ΔT syndrome in a hot and humid climate. *Sci Technol Built Environ*. 2017;23:582–593.
260. Gorsuch EL, Grinshpun SA, Willeke K, Reponen T, Moss CE, Jensen PA. Method for Evaluating Germicidal Ultraviolet Inactivation of Biocontaminated Surfaces. *Int J Occup Saf Ergon*. 1998;4:287–297.
261. Buonanno M, Welch D, Shuryak I, Brenner DJ. Far-UVC light (222 nm) efficiently and safely inactivates airborne human coronaviruses. *Sci Rep*. 2020;10:10285.
262. Yamano N, Kunisada M, Kaidzu S, et al. Long-term Effects of 222-nm ultraviolet radiation C Sterilizing Lamps on Mice Susceptible to Ultraviolet Radiation. *Photochem Photobiol*. 2020;96:853–862.
263. Claus H. Ozone Generation by Ultraviolet Lamps. *Photochem Photobiol*. 2021;97:471–476.
264. Miller SL, Linnes J, Luongo J. Ultraviolet Germicidal Irradiation: Future Directions for Air Disinfection and Building Applications. *Photochem Photobiol*. 2013;89:777–781.

265. Wang C, Holmberg S, Sadrizadeh S. Numerical study of temperature-controlled airflow in comparison with turbulent mixing and laminar airflow for operating room ventilation. *Build Environ*. 2018;144:45–56.
266. Ai Z, Hashimoto K, Melikov AK. Airborne transmission between room occupants during short-term events: Measurement and evaluation. *Indoor Air*. 2019;29:563–576.
267. Bhagat RK, Wykes MSD, Dalziel SB, Linden PF. Effects of ventilation on the indoor spread of COVID-19. *J Fluid Mech*. 2020;903. November 2020.
<https://www.cambridge.org/core/journals/journal-of-fluid-mechanics/article/effects-of-ventilation-on-the-indoor-spread-of-covid19/CF272DAD7C27DC44F6A9393B0519CAE3>. Accessed May 6, 2021.
268. Bjørn E, Nielsen PV. Dispersal of exhaled air and personal exposure in displacement ventilated rooms: **Dispersal of exhaled air and personal exposure in displacement ventilated rooms**. *Indoor Air*. 2002;12:147–164.
269. Villafruela JM, Olmedo I, Berlanga FA, Ruiz De Adana M. Assessment of displacement ventilation systems in airborne infection risk in hospital rooms. *PLOS ONE*. 2019;14:e0211390.
270. Nielsen PV, Buus M, Winther FV, Thilageswaran M. Contaminant Flow in the Microenvironment Between People Under Different Ventilation Conditions. *ASHRAE Trans*. 2008;114:632–638.
271. Singer BC, Zhao H, Preble CV, et al. Measured influence of overhead HVAC on exposure to airborne contaminants from simulated speaking in a meeting and a classroom. *Indoor Air*. n/a.
<https://onlinelibrary.wiley.com/doi/abs/10.1111/ina.12917>. Accessed October 20, 2021.
272. Zhou Q, Qian H, Ren H, Li Y, Nielsen PV. The lock-up phenomenon of exhaled flow in a stable thermally-stratified indoor environment. *Build Environ*. 2017;116:246–256.
273. Nazaroff WW. Indoor particle dynamics. *Indoor Air*. 2004;14:175–183.
274. Thatcher TL, Lai ACK, Moreno-Jackson R, Sextro RG, Nazaroff WW. Effects of room furnishings and air speed on particle deposition rates indoors. *Atmos Environ*. 2002;36:1811–1819.
275. Jeong J-W, Bem J, Bahnfleth WP, Freihaut JD, Thran B. Critical Review of Aerosol Particle Transport Models for Building HVAC Ducts. *J Archit Eng*. 2009;15:74–83.
276. Sippola MR, Nazaroff WW. Experiments Measuring Particle Deposition from Fully Developed Turbulent Flow in Ventilation Ducts. *Aerosol Sci Technol*. 2004;38:914–925.
277. Siegel J, Walker I. *Deposition of Biological Aerosols on HVAC Heat Exchangers*. Lawrence Berkeley National Laboratory; 2001:13.
278. Boone SA, Gerba CP. Significance of fomites in the spread of respiratory and enteric viral disease. *Appl Environ Microbiol*. 2007;73:1687–1696.
279. Bramwell L, Qian J, Howard-Reed C, Mondal S, Ferro AR. An evaluation of the impact of flooring types on exposures to fine and coarse particles within the residential micro-environment using CONTAM. *J Expo Sci Environ Epidemiol*. 2016;26:86–94.

280. Haines SR, Adams RI, Boor BE, et al. Ten questions concerning the implications of carpet on indoor chemistry and microbiology. *Build Environ.* 2020;170:106589.
281. Karlsson E, Berglund T, Strömqvist M, Nordstrand M, Fängmark I. The effect of resuspension caused by human activities on the indoor concentration of biological aerosols. *J Aerosol Sci.* 1999;30:S737–S738.
282. Khare P, Marr LC. Simulation of vertical concentration gradient of influenza viruses in dust resuspended by walking. *Indoor Air.* 2015;25:428–40.
283. Qian J, Peccia J, Ferro AR. Walking-induced particle resuspension in indoor environments. *Atmos Environ.* 2014;89:464–481.
284. Qian J, Ferro AR. Resuspension of Dust Particles in a Chamber and Associated Environmental Factors. *Aerosol Sci Technol.* 2008;42:566–578.
285. Salimifard P, Rim D, Gomes C, Kremer P, Freihaut JD. Resuspension of biological particles from indoor surfaces: Effects of humidity and air swirl. *Sci Total Environ.* 2017;583:241–247.
286. Zhou B, Zhao B, Tan Z. How Particle Resuspension from Inner Surfaces of Ventilation Ducts Affects Indoor Air Quality—A Modeling Analysis. *Aerosol Sci Technol.* 2011;45:996–1009.
287. Li Y, Huang X, Yu ITS, Wong TW, Qian H. Role of air distribution in SARS transmission during the largest nosocomial outbreak in Hong Kong. *Indoor Air.* 2005;15:83–95.
288. Qian H, Li Y, Nielsen PV, Huang X. Spatial distribution of infection risk of SARS transmission in a hospital ward. *Build Environ.* 2009;44:1651–1658.
289. Xiao S, Tang JW, Hui DS, Lei H, Yu H, Li Y. Probable transmission routes of the influenza virus in a nosocomial outbreak. *Epidemiol Infect.* 2018;146:1114–1122.
290. Kim S-H, Chang SY, Sung M, et al. Extensive viable middle east respiratory syndrome (MERS) coronavirus contamination in air and surrounding environment in MERS isolation wards. *Clin Infect Dis.* 2016;63:363–369.
291. Huang J, Jones P, Zhang A, Hou SS, Hang J, Spengler JD. Outdoor Airborne Transmission of Coronavirus Among Apartments in High-Density Cities. *Front Built Environ.* 2021;7. 2021. <https://www.frontiersin.org/articles/10.3389/fbuil.2021.666923/full>. Accessed June 10, 2021.
292. Hwang SE, Chang JH, Oh B, Heo J. Possible aerosol transmission of COVID-19 associated with an outbreak in an apartment in Seoul, South Korea, 2020. *Int J Infect Dis IJID Off Publ Int Soc Infect Dis.* 2021;104:73–76.
293. Lin G, Zhang S, Zhong Y, et al. Community evidence of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) transmission through air. *Atmos Environ.* 2021;246:118083.
294. ASHRAE Epidemic Task Force. Core recommendations for reducing airborne infectious aerosol exposure. January 2021. January 6, 2021. <https://www.ashrae.org/file%20library/technical%20resources/covid-19/core-recommendations-for-reducing-airborne-infectious-aerosol-exposure.pdf>.

295. Bohac DL, Hewett MJ, Hammond SK, Grimsrud DT. Secondhand smoke transfer and reductions by air sealing and ventilation in multiunit buildings: PFT and nicotine verification. *Indoor Air*. 2011;21:36–44.
296. Grosskopf K, Lautz R, Mousavi-Rizi E, Lau J. *Ventilation in Residential Care Environments*. US Department of Energy Office of Energy Efficiency and Renewable Energy; 2021:78.
297. Khan TR, Parker DS, Withers C. Mitigation of Airborne Contaminant Spread through Simple Interventions in an Occupied Single-Family Home. *Int J Environ Res Public Health*. 2021;18:5880.
298. Miller SL, Clements N, Elliott SA, Subhash SS, Eagan A, Radonovich LJ. Implementing a negative-pressure isolation ward for a surge in airborne infectious patients. *Am J Infect Control*. 2017;45:652–659.
299. Sudre CH, Murray B, Varsavsky T, et al. Attributes and predictors of long COVID. *Nat Med*. 2021;27:626–631.
300. Song DJ. Rhinovirus and childhood asthma: an update. *Korean J Pediatr*. 2016;59:432–439.
301. Fisk WJ, Mirer AG, Mendell MJ. Quantitative relationship of sick building syndrome symptoms with ventilation rates. *Indoor Air*. March 2009:7.
302. Seppänen OA, Fisk W. Some Quantitative Relations between Indoor Environmental Quality and Work Performance or Health. *HVACR Res*. 2006;12:957–973.
303. Hughes SC, Bellettiere J, Nguyen B, et al. Randomized Trial to Reduce Air Particle Levels in Homes of Smokers and Children. *Am J Prev Med*. 2018;54:359–367.
304. Jhun I, Gaffin JM, Coull BA, et al. School Environmental Intervention to Reduce Particulate Pollutant Exposures for Children with Asthma. *J Allergy Clin Immunol Pract*. 2017;5:154-159.e3.
305. Montgomery JF, Reynolds CCO, Rogak SN, Green SI. Financial implications of modifications to building filtration systems. *Build Environ*. 2015;85:17–28.
306. Park J-H, Lee TJ, Park MJ, Oh H, Jo YM. Effects of air cleaners and school characteristics on classroom concentrations of particulate matter in 34 elementary schools in Korea. *Build Environ*. 2020;167:106437.
307. Polidori A, Fine PM, White V, Kwon PS. Pilot study of high-performance air filtration for classroom applications. *Indoor Air*. 2013;23:185–195.
308. Satish U, Mendell MJ, Shekhar K, et al. Is CO₂ an Indoor Pollutant? Direct Effects of Low-to-Moderate CO₂ Concentrations on Human Decision-Making Performance. *Environ Health Perspect*. 2012;120:1671–1677.
309. Wu J, Weng J, Xia B, Zhao Y, Song Q. The Synergistic Effect of PM_{2.5} and CO₂ Concentrations on Occupant Satisfaction and Work Productivity in a Meeting Room. *Int J Environ Res Public Health*. 2021;18.

310. Milton DK, Glencross PM, Walters MD. Risk of sick leave associated with outdoor air supply rate, humidification, and occupant complaints. *Indoor Air*. 2000;10:212–221.
311. Shendell DG, Prill R, Fisk WJ, Apte MG, Blake D, Faulkner D. Associations between classroom CO₂ concentrations and student attendance in Washington and Idaho. *Indoor Air*. 2004;14:333–341.
312. Fisk WJ, Black D, Brunner G. Benefits and costs of improved IEQ in U.S. offices. *Indoor Air*. 2011;21:357–367.
313. Rim D, Schiavon S, Nazaroff WW. Energy and cost associated with ventilating office buildings in a tropical climate. *PLoS One*. 2015;10:e0122310.
314. Mendell MJ, Fisk WJ, Kreiss K, et al. Improving the Health of Workers in Indoor Environments: Priority Research Needs for a National Occupational Research Agenda. *Am J Public Health*. 2002;92:1430–1440.
315. Jacot D, Greub G, Jaton K, Opota O. Viral load of SARS-CoV-2 across patients and compared to other respiratory viruses. *Microbes Infect*. 2020;22:617–621.
316. Cheng Y, Ma N, Witt C, et al. Face masks effectively limit the probability of SARS-CoV-2 transmission. *Science*. May 2021. May 20, 2021.
<https://science.sciencemag.org/content/early/2021/05/19/science.abg6296>. Accessed June 10, 2021.
317. Brundage JF, Scott RM, Lednar WM, Smith DW, Miller RN. Building-associated risk of febrile acute respiratory diseases in Army trainees. *JAMA*. 1988;259:2108–2112.
318. Hoge CW, Reichler MR, Dominguez EA, et al. An epidemic of pneumococcal disease in an overcrowded, inadequately ventilated jail. *N Engl J Med*. 1994;331:643–648.
319. Menzies D, Fanning A, Yuan L, FitzGerald JM. Factors Associated with Tuberculin Conversion in Canadian Microbiology and Pathology Workers. *Am J Respir Crit Care Med*. February 2003.
320. Sun Y, Wang Z, Zhang Y, Sundell J. In China, Students in Crowded Dormitories with a Low Ventilation Rate Have More Common Colds: Evidence for Airborne Transmission. Semple MG, ed. *PLoS ONE*. 2011;6:e27140.
321. Killingley B, Enstone JE, Groatorex J, et al. Use of a human influenza challenge model to assess person-to-person transmission: proof-of-concept study. *J Infect Dis*. 2012;205:35–43.
322. Hierarchy of Controls | NIOSH | CDC. June 17, 2020.
<https://www.cdc.gov/niosh/topics/hierarchy/default.html>. Accessed March 28, 2021.
323. Brooks JT. Maximizing Fit for Cloth and Medical Procedure Masks to Improve Performance and Reduce SARS-CoV-2 Transmission and Exposure, 2021. *MMWR Morb Mortal Wkly Rep*. 2021;70.
324. Leith D, L'Orange C, Volckens J. Quantitative Protection Factors for Common Masks and Face Coverings. *Environ Sci Technol*. 2021;55:3136–3143.

325. Leung NHL, Chu DKW, Shiu EYC, et al. Respiratory virus shedding in exhaled breath and efficacy of face masks. *Nat Med*. April 2020.
326. Lindsley WG, Blachere FM, Law BF, Beezhold DH, Noti JD. Efficacy of face masks, neck gaiters and face shields for reducing the expulsion of simulated cough-generated aerosols. *Aerosol Sci Technol*. 2021;55:449–457.
327. Brooks JT, Butler JC. Effectiveness of Mask Wearing to Control Community Spread of SARS-CoV-2. *JAMA*. 2021;325:998.
328. Cheng VC-C, Wong S-C, Chuang VW-M, et al. The role of community-wide wearing of face mask for control of coronavirus disease 2019 (COVID-19) epidemic due to SARS-CoV-2. *J Infect*. 2020;81:107–114.
329. Gandhi M, Beyrer C, Goosby E. Masks Do More Than Protect Others During COVID-19: Reducing the Inoculum of SARS-CoV-2 to Protect the Wearer. *J Gen Intern Med*. July 2020.
330. Gandhi M, Marr LC. Uniting Infectious Disease and Physical Science Principles on the Importance of Face Masks for COVID-19. *Med*. 2021;2:29–32.
331. Liang M, Gao L, Cheng C, et al. Efficacy of face mask in preventing respiratory virus transmission: A systematic review and meta-analysis. *Travel Med Infect Dis*. 2020;36:101751.
332. AIHA. Reopening: guidance for schools (K-12) V3. December 2020.
333. Stewart EJ, Schoen LJ, Mead K, et al. *ASHRAE Position Document on Infectious Aerosols*. Atlanta, GA: ASHRAE; 2020:24.
334. ASHRAE Epidemic Task Force. Reopening schools and university guidance. July 2020.

Tables

Table 1. Scales of infectious aerosol transfer in buildings and associated engineering controls

	Close-interactive scale	Room scale	Building scale
Scale description	Interactions within 1-2 m, occurring for at least 15 min per 24 h. Interactions include conversing, eating, laughing, working, and other. Risk increases with source emission and susceptible person inhalation rate, both related to activity. Risk increases with duration.	Exposure within-room, between individuals not having close-interactive transfer. Poses the greatest risk for superspreading given potential large numbers of exposed and high concentrations of infectious aerosol when uncontrolled.	Exposure between rooms or floors in a building with air transfer occurring through forced air heating, ventilating, and air conditioning (HVAC) systems or through pressure-induced airflow via connections including internal doorways and halls, plumbing, or common exhaust fan inlets.
Ventilation and airflow management	<ul style="list-style-type: none"> • Workstation airflow management. • Room-scale directional airflow. 	<ul style="list-style-type: none"> • Increase clean air delivery. • Directional airflow and clean air supply to the breathing zone. • Multi-zone HVAC systems (increase mixing volume and decrease high concentration transfer when an infected person is in the room). 	<ul style="list-style-type: none"> • Increase clean air delivery. • Directional airflow, e.g., exhausting from rooms expected to have greater presence of infectious aerosol.
Filtration by HVAC system	<ul style="list-style-type: none"> • Increase clean air delivery via in-duct filtration. Must mix with breathing zone air. 	<ul style="list-style-type: none"> • Increase in-room clean air delivery via in-duct filtration. 	<ul style="list-style-type: none"> • Increase clean air delivery with multi-zone sources via in-duct filtration.
Filtration by portable air cleaner	<ul style="list-style-type: none"> • Applied near the breathing zone (could be part of workstation airflow management). • Personal air cleaning devices. 	<ul style="list-style-type: none"> • Applied near the breathing zone and/or throughout the space. 	<ul style="list-style-type: none"> • Approaches from other scales.
Infectious aerosol inactivation by GUV	<ul style="list-style-type: none"> • Far GUV (222nm wavelength) in the breathing zone. 	<ul style="list-style-type: none"> • Far GUV in the breathing zone and/or throughout room space. • Upper-room GUV (best with induced mixing of air to upper-room). • GUV in recirculating HVAC ducts. 	<ul style="list-style-type: none"> • Approaches from other scales.
Other strategies	<ul style="list-style-type: none"> • Physical barriers (more helpful for drop sprays and larger aerosols compared with smaller aerosols). 	<ul style="list-style-type: none"> • Flushing between occupant cohorts 	<ul style="list-style-type: none"> • Sealing openings between spaces

Table 2. Settings with elevated risk factors for infectious aerosol transmission

Priority settings (examples)	Potential risk factors related to activities done in the setting leading to exposure at room scale and sometimes close-interactive and/or building scale
<u>Dining</u> (school cafeteria, restaurant, institutional residential, event)	Impractical to wear masks; close-interactive; conversation, laughter; moderate duration (0.5–1 h) per encounter and possibly multiple encounters during infectious period; people moving makes directional airflow control challenging; many restaurants intended for high density occupancy; break rooms and dining areas may not be easily separable from mixing with other occupied areas, e.g., in schools, offices, and institutional residential buildings.
<u>Risky occupational settings</u> (slaughterhouse, meat packing, factory, call center, agricultural worker housing)	Long duration of co-occupancy over multiple days; conversation and loud speech may be required; PPE may not be available, may be uncomfortable to use, or poorly fitted; masking adherence may be problematic, especially in warm environments; special risks associated with some settings (e.g., talking at call centers, workstations that cannot be easily distanced, low temperature and relative humidity in meat processing plants); low ventilation; workers often limited to raise concerns; co-workers with elevated risk from living in high density homes with others also working in high risk occupational settings; limited/no paid leave discourages self-isolation/quarantine.
<u>Schools, meetings</u> (preschool, K-12, university, conference, classroom, dining hall, gym, auditorium)	Classrooms commonly have high occupant density, long periods of co-occupancy over consecutive days; loud speech often required for communication; conversations and small group interactions between classes and in halls are common; many facilities are older, with low ventilation or filtration in HVAC systems; students may have higher-risk living situations, e.g., sharing high-density housing with parents who work in high risk jobs; limited adherence to distancing and masking; limited or no access to respirators.
<u>Local & regional public transit</u> (train, bus, car sharing)	Economic viability of local and regional transit often depends on high rider densities during peak commutes; difficult to enforce mask rules and masks may not be correctly fitted or worn; screening is infeasible; co-occupancy with potentially large groups of strangers with unknown exposure for 0.5–1 h or more; limited or no access to respirators.
<u>Institutional residential</u> (dormitory, nursing home, long-term care, prison, shelter, military barrack)	Constant occupancy or for many hours per day; masking of residents is often infeasible; frequency and volume of conversation often cannot be controlled; close interactions between staff and residents needing care; many older facilities with inadequate ventilation and filtration; shared bedrooms; airflow connections between bedrooms and between dining areas and other common areas; natural ventilation often not practical; staff may work at multiple institutions and introduce infection between settings; residents may have comorbidities; worse conditions for underserved communities; limited or no access to respirators.
<u>Grocery, retail</u>	Employees exposed to large population (potentially infectious), close-interactive (e.g., cashier), long duration of workday exposure; infeasible to screen customers; some stores have small volume, narrow aisles, low ventilation; employees may not have paid sick leave; small businesses may not have enough staff to encourage staying home for infection control; limited or no access to respirators.
<u>Oratory, singing, wind instrument, performance</u> (rehearsal room, performance hall, religious gathering)	Many people present (potential for superspreading) and often high density; close-interactive; performers may be less likely to wear masks (e.g., film production), and are likely to use loud speech, shouting, or singing.
<u>Offices</u>	Conference rooms or similar space could host room-scale exposure for many people over a prolonged period of time (hours per day, over months); close interactions; limited or no access to respirators.
<u>Athletics performance</u> (fitness facility, playing field/court, spectator area)	Many people present; typically without face masks; close-interactive (among players, among spectators), loud speech, shouting, increased heavy breathing; building scale transfer from strong source generation.
<u>Private residential</u> (single- or multi-unit housing)	Constant occupancy or exposure for many hours each day; close-interactive; masks typically not worn; inadequate ventilation in many homes, especially when hot or cold outside; often higher density in underserved communities; toilet-generated aerosols; potential airflow connections between apartments, spanning multiple floors (e.g., shared HVAC, stack-driven flows in converted single-family residence, exhaust ventilation in multi-story building).
<p>There are variations possible in each setting, and risk of transmission is related to multiple elements, including:</p> <ol style="list-style-type: none"> 1. Number of potentially infectious people present 2. Number of people present with elevated immune susceptibility and risk of severe illness 3. Distancing and density of people in the indoor space 4. Use of face mask for emissions control 5. Use of PPE (including face masks, but especially N95 or equivalent filtering facepiece respirators) 6. Duration of exposure 7. Magnitude of respiration (speaking, speaking loudly or shouting, singing, breathing fast and/or heavy) 8. Presence of mechanical ventilation 9. Presence of filtration or GUV in forced air HVAC system 10. Differential burdens of exposures that increase risk for underserved socioeconomic and demographic groups 	

Table 3. Epidemiologic studies that evaluate the effect of ventilation on infection risk

Study	Exposure scenario	Infection assessment	Ventilation assessment	Ventilation comparison	Risk of infection ^a
³¹⁷ (Brundage et al., 1988)	Army trainees living in close quarters in barracks over 47 months.	Retrospective records assessment for febrile ($\geq 38^{\circ}\text{C}$) respiratory illness.	Estimated based on barrack design and occupancy ⁵⁶ .	0.9 vs 6.8 L/s/p; 'Modern', tighter sealed versus older, 'leaky' barracks.	Adjusted risk ratio 1.51 (95% CI 1.46-1.56).
³¹⁸ (Hoge et al., 1994)	Inmates living in different areas of a jail over 4 weeks during an <i>S. pneumoniae</i> outbreak.	Prospective culture of respiratory swabs & serology for <i>S. pneumoniae</i> .	Cross-sectional measurement of CO ₂ and evaluation of air flow from the ventilation system.	>3.4 vs 2.0 L/s/p; Cell block style with more vs less outside air.	Adjusted odds ratio 2.02 (95% CI 1.07-3.82).
^{202(p200)} (Menzies et al., 2000)	Health care workers exposed to TB cases over 3 years.	Cross-sectional analysis of tuberculin skin test (TST) conversion.	Cross-sectional CO ₂ decay and smoke release experiments.	<2 vs ≥ 2 ACH; workers in lower versus higher ventilated spaces.	Adjusted hazard ratio 3.4 (95% CI 2.1-5.8) for TST conversion negative to positive.
³¹⁹ (Menzies, et al., 2003)	Laboratorians working in hospitals with TB cases over 3 years.	Cross-sectional analysis of tuberculin skin test conversion.	Cross-sectional CO ₂ decay and smoke release experiments.	16.7 vs 32.5 ACH (averages); lower versus higher ventilated spaces.	Unadjusted infection risk greater ($p < 0.001$; unpaired t test).
³²⁰ (Sun et al., 2011)	University dormitory population in 17 buildings.	Questionnaire of common cold incidence over the previous year.	Cross-sectional measurement of CO ₂ decay experiments (peak vs outdoor).	5 vs 1 L/s/p; Average dorm room ventilation rate of (CO ₂ decay calculation).	Incident risk ratio 7 (35% versus 5% study population) for ≥ 6 common colds.
¹⁹⁷ (Du et al., 2020)	Retrospective cohort of household and university campus contacts (at least 30 hours of shared air) of infectious TB cases from an outbreak. Ventilation interventions applied.	Sputum tests and chest x-ray to detect active TB cases, with sequencing to confirm probable transmission clusters.	Measured CO ₂ concentrations before and after intervention.	>1,000 vs <1,000 ppm CO ₂ (pre- vs post-intervention classroom) with exposure to cases; CO ₂ ppm (estimated clean air flow L/s/p) were 3,200 (1.7) & 600 (23.6-25.1).	Adjusted hazard ratio 32.8 (95% CI 2.0-540.3) for acquiring active TB infection.
²⁰³ (Zhu et al., 2020)	University dormitory population in 'low' (LVB) and 'high ventilated' (HVB) dormitory buildings.	Prospective symptom monitoring with qRT-PCR for acute respiratory infections.	Continuous measurement of CO ₂ >5 mo. Measurement of building envelope pressure and local weather data.	2.0 vs 5.9 L/s/p; LVB vs HVB participant room means. 1.9 vs 2.1 L/s/p; leeward vs windward room means in LVB.	Unadjusted incident rate ratio 4.04 (95% CI 0.69-163.02) LVB vs HVB; 1.3 (0.7-2.61) leeward vs windward.
³²¹ (proof-of-concept [POC], Killingley et al., 2012); ²¹¹ (main study, Nguyen-Van-Tam et al., 2020)	Compared infection rate between 2 human challenge trials with different ventilation levels.	Daily, upper respiratory swab sample following inoculation, and pre- vs post-infection serology.	POC estimated given sealed suite with bathroom exhaust ¹⁷⁴ . Main estimated by CO ₂ decay & tracer gas experiments.	0.8 L/s/p vs 4 L/s/p; POC vs main study.	Unadjusted risk ratio of transmission 6.4 (8.3 vs 1.3%).
^a Exposure is compared at lower vs higher ventilation level.					

Appendices

Appendix 1

Table A1. Tools for estimating exposure or risk for SARS-CoV-2 in indoor environments

Tool/Source	Key parameters that can be manipulated
Safe Air Spaces Oregon Institute for Health in the Built Environment	Risk of SARS-CoV-2 transmission considers “high” or “low” viral emitter, number of occupants sharing air, ventilation, extra air cleaning from filtration.
Portable Air Cleaner Calculator for Schools v1 Harvard-CU Boulder	Considers the number of people and size of space, and risk of SARS-CoV-2 transmission; provides suggestion for how to increase effective air exchange rate through use of portable air cleaning devices.
COVID-19 Aerosol Transmission Estimator Jose Jiménez CU-Boulder	Aerosol transmission calculator. Considers infectious dose emission rate (quanta), inhalation rate, mask efficiencies for source, control and PPE, building ventilation rate, biological decay of virus and aerosol deposition onto surfaces, chance of encountering an infectious person, proportion of population immune. Visualization by El País using the Jiménez aerosol transmission estimator.
Estimation of COVID-19 infection risk from airborne transmission during classroom teaching Duke University	Adding probabilistic Monte Carlo approach to Jose Jiménez transmission risk estimator.
Airborne infection risk calculator International collaborators (USA, Italy, Australia), hosted by CUNY	Estimates risk as a function of time, viral inactivation/removal, room volume, number of infectious occupants, breathing level based on activity, and estimated quanta generation level based on comprehensive analysis of published findings.
COVID-19 Risk Calculator Harvard Healthy Buildings	Estimates risk based on model described in analysis of Diamond Princess cruise ship outbreak. Model adjusts risk based on room size, length of exposure, activity type, and controls including face mask use, distancing, ventilation, air cleaning, hand washing, and room cleaning.
FaTIMA (Fate and Transport of Indoor Microbiological Aerosols) NIST	Multizone modeling tool to help predict viral aerosol exposure given exposure within a building. Considers ventilation from building infiltration and mechanical sources, system filtration, portable air cleaner use. Describes exposure and does not make assumptions about the relationship between exposure and infection risk. (Documentation)
Equivalent outdoor air calculator ASHRAE	Estimates total equivalent air changes per hour in a space and the flush-out time to achieve 3 air changes per hour. The goal of the flush-out is to reduce exposure to contaminants that build up over time with occupants.
Ventilation calculator REHVA	Estimates the effect of ventilation on SARS-CoV-2 transmission risk.
COVID Exposure Assessment Tool (CEAT) Signature Science, LLC	Considers near-field and far-field exposure associated with numerous factors, including community infection prevalence and adherence to distancing measures. Benchmarks risk associated with inhalation exposure using OSHA “high risk” classification.

seco-Tool Michael Riediker and Christian Monn; SECO (Swiss State Secretariat for Economic Affairs)	Calculates concentration of aerosolized virus in a room and exposure within an arm's length (60cm) and at room-scale. Considers mask use, variable source emission, physical activity, speech, and room size, air exchange, and air flow velocity.
Facility Infection Risk Estimator v2.1 BranchPattern	Estimates number of infected adults and children per exposure scenario. Can build exposure scenarios based on age, activity level, room size, use of GUV, air exchange, filtration, exposure time, level of viral shedding into exhaled breath, mask use. Translates disease estimates into economic value, and associated, hypothetical reproductive ratio values.
Why Is the Risk of Coronavirus Transmission so High Indoors? Article with visualization and tool . Zeit Online Publication with advising from a Max Planck Institute for Chemistry research team (Jos Lelieveld et al. 2020)	Estimates transmission given available evidence and assumptions regarding generation of infectious aerosols including through speech, speech volume, singing, coughing, mask efficiency, room size, air exchange rate, and occupancy density, and length of exposure. The concentration of infectious virus contained in respiratory lining fluid is used to estimate infectious material concentration in aerosols. Measured concentrations of exhaled breath particles are used.
An analysis of three Covid-19 outbreaks: how they happened and how they can be avoided. El Pafis in collaboration with numerous public health agencies advising.	Provides visual models of documented transmission of SARS-CoV-2 in an office, a restaurant, and a bus. Provides suggestion for mitigating transmission based on the hierarchy of controls.
City reduced probability of infection for indoor airborne transmission of COVID-19. Concordia	Draws on the Jiménez transmission estimator and building archetypes to infer infection transmission risk at the building level across Canada and the United States.

Appendix 2: Details of the aerosol transfer model in an office

A CONTAM simulation was performed to estimate respiratory aerosol concentrations a) in the infector subzone (close-interactive transfer), b) in a well-mixed room space occupied by the infector, that is supplied by, separately, SZ and MZ HVAC systems, and c) in a separate room connected by the MZ system (described in main text). The schematic for the MZ and SZ simulations showing airflows and aerosol deposition is given by Figure A1. The filtration efficiencies of the MERV13 filter and MERV8-like cloth masks for each aerosol size bin used in the model are given by Table A2. We used a mass balance approach to compute respiratory aerosol concentrations mediated by pressure and flow in the theoretical office space at the transfer scales of interest, described by

$$\frac{dC_i}{dt} = \frac{\dot{S}_i}{V} - \left(\lambda + \kappa_i + (1 - OA) \frac{Q_{HVAC}}{V} \eta_i \right) C_i, \quad (3)$$

where subscript i denotes respiratory droplet size bin, with C respiratory aerosol droplet concentration (number or volume) in air, \dot{S} respiratory aerosol number generation strength, V indoor space volume, λ ventilation rate, κ deposition rate, OA outdoor air fraction, Q_{HVAC} HVAC mechanical flow rate, and η filter efficiency. One minute injections of source aerosol were considered in the simulation for 60 consecutive minutes with constant HVAC air delivery. Details to guide reproduction of the CONTAM simulation are described at https://gitlab.com/jacobbueno/building_controls_for_infectious_aerosols.

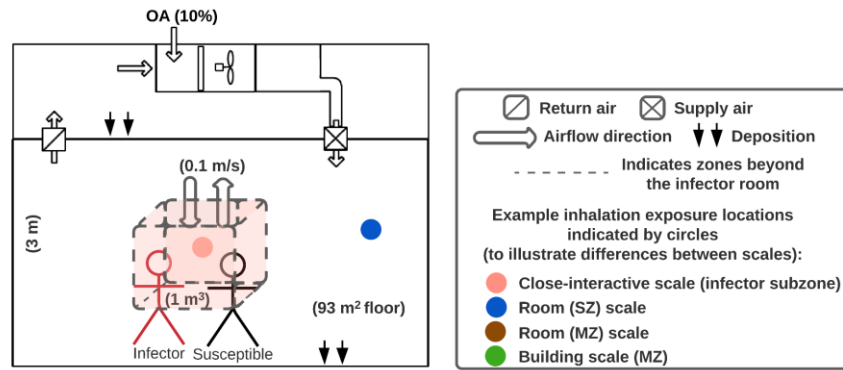
Figure A2 depicts the volume (top panel) and aerosol particle number (bottom panel) concentrations at each scale of transfer. As expected, and based on Figure 1 (main text), the concentrations of respiratory aerosols are higher in the close-interactive scale (SZ infector subzone space), compared with the other aerosol transfer scales. Based on the available knowledge of respiratory aerosols generated during speech (Table A1)^{82,177}, the model predicts the highest volume concentrations for the close-interactive and room scale exposures at the upper end of the modeled particle diameters of approximately 14 μm . It predicts the highest number concentration for all scales at approximately 1 μm . A single \log_{10} increase in diameter corresponds with a 3 \log_{10} increase in volume for an aqueous sphere. The volume and number concentrations drop sharply at approximately 5 μm for the building scale transfer, due to an increasing role of deposition in removal, suggesting a meaningful role of deposition in the lower building scale transfer compared with the other scales.

Table A2. Input values for CONTAM model

Equilibrated size	Initial size	Number Distribution ^a (released / min)	Deposition ^b (% removed / h)	MERV 13	Mask filtration efficiency (% particles captured)	
					Out-Flow	In-Flow
0.3	0.5–1.0	74	1.20E-01	0.498	39.94	21.74
0.6	1–2	1129	6.00E-02	0.528	57.81	30.92
1.2	2–4	1176	2.80E-01	0.592	71.66	52.18
2.4	4–8	537	0.84996	0.754	81.97	67.79
4.8	8–16	133	2.30004	0.953	87.14	78.75
8	16–24	48	4.5	0.990	87.14	85.04
11.2	24–32	34	8.1	0.995	87.14	87.14
14.4	32–40	31	12.9996	0.998	87.14	87.14

^a For continuous speaking. ^b Deposition on surfaces in the room and in the HVAC system.

SZ Schematic



MZ Schematic

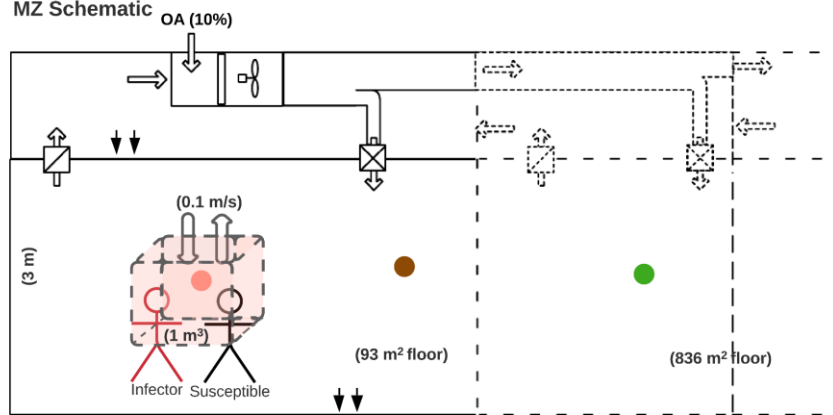


Figure A1. Model schematics. Single zone (SZ; top panel) and multizone (MZ; bottom panel) aerosol transfer model office spaces.

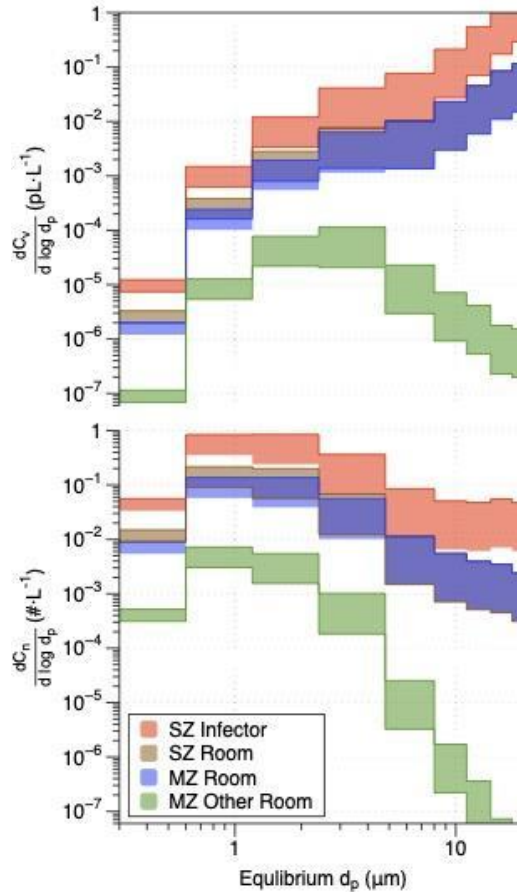


Figure A2. Volume and number concentrations at scales of transfer by equilibrated respiratory aerosol size. The volume concentration distribution by equilibrated particle size is given in pL respiratory volume per L air (top panel). The number concentration distribution by equilibrated particle size is the number of aerosol particles per L air (bottom panel). The eight equilibrated particle size bins correspond to those in Table A2. The top band of each shaded region corresponds to an unmasked scenario (no mask on both infector and susceptible) and the bottom band corresponds to a scenario where both infector and susceptible are wearing cloth masks.

Appendix 3: Source control and personal protective equipment (PPE)

Reduce the chances of an infectious person being present

Reducing or eliminating the source of a hazard is the most effective approach per the hierarchy of controls³²². For airborne pathogens, the aim is to reduce the chance that an infectious person will enter a communal indoor space; and if they do enter, to minimize their emissions. This approach is particularly challenging when asymptomatic individuals can transmit infectious quanta, as occurs with SAR-CoV-2^{44,45,47}. Source controls include capacity and duration limits, symptom screening, contact and risk factor questionnaires to identify those with recent exposure in high risk settings, frequent testing, separation of cohorts (e.g., via scheduling in school) to limit contacts, and ventilation flushing or air cleaning via filtration or GUV between sequential occupancies of indoor spaces.

Reduce emissions from infectious occupants

Source control aims to reduce the release of infectious aerosols, sprays, or surface contamination to interrupt transmission modes when infectious status is known or unknown, works across all scales of control, and can enable lower risk even when other controls may be inadequate. Activity control, including reducing vocalization, shouting, singing, activities that elicit heavy breathing, can reduce the quantity of infectious aerosols generated, as described earlier. Face masks have demonstrated effectiveness at reducing the release of infectious aerosols of various sizes of concern for inhalation exposures ^{98,323–326}. In addition to their filtering capacity, face masks also reduce the velocity of expired air streams, thus reducing the likelihood of direct transfers of infectious aerosols at high concentrations. Aerosols that escape a face mask often become entrained in thermal plumes rising upward out of the breathing zone, although natural ventilation or mechanically driven air movement also influence aerosol dispersal and transport. It is unclear how respirators with exhalation valves affect respiratory jets, although they are likely to reduce outward velocities to some degree. Face mask use among the public has been characterized as an effective layer of protection against SARS-CoV-2 community transmission ^{327–330}.

Reduce exposure with PPE

Individuals who spend time in settings with known or potential risk can use PPE to reduce or eliminate exposure to infectious aerosols, ballistic drops, and contaminated surfaces. Face masks can serve as PPE, reducing inhalation exposure to infectious aerosols ⁶⁷. The effect can be increased if multiple layers are used and the seal around the face is tightened ³²³. Given that SARS-CoV-2 genomes have been detected in aerosols in PPE doffing areas ⁹², care should be taken to protect against doffing-associated exposure that could lead to infection. A meta-analysis of epidemiologic studies showed associations with surgical mask or respirator use with reduced infection risk of approximately half or more in healthcare and non-healthcare settings ³³¹. There still can be substantial risk of infection via aerosols despite surgical mask use, as has been noted in healthcare settings ¹⁶⁶, which could be mitigated by well-fitted respirators that more effectively reduce aerosol inhalation ¹⁶⁷. Some epidemiological studies showed a protective effect of eye protection ¹⁶⁵.

Appendix 4: Guidelines regarding building ventilation

Organizations have provided guidance for ventilation to control respiratory infections, and recently, SARS-CoV-2 (e.g., <http://ashrae.org/covid19>). There has been widespread acknowledgement of infectious aerosols contributing to the spread of infection epidemic, which has spurred efforts to advise building operators on infection control actions. Given the challenges of developing precise ventilation standards to effectively reduce airborne infection (specific beyond “more ventilation is better”), the collective wisdom of infectious disease experts and building engineers generally emphasizes some level of increased ventilation to mitigate SARS-CoV-2 spread, while maintaining thermal comfort, to reduce airborne transmission risk ^{40,332,333}. Upgrading HVAC filters to MERV13 or better, using portable air cleaners (with MERV13 filters or better), and using upper room germicidal UV (GUV) are also suggested to enhance infection control.

The Federation of European Heating, Ventilation, and Air Conditioning Associations (REHVA) recommends airborne infection isolation rooms (AIIR) to have at least 6–12 ACH, with new

builds having ≥ 12 ⁴⁰. REHVA suggests upgrading ventilation in any healthcare wards with infectious disease cases to match AIIR levels, and at least 4 ACH in other zones of healthcare facilities. The American Society of Heating, Refrigeration, and Air-Conditioning Engineers (ASHRAE) goes beyond this in Standard 170, advising at least 12 ACH in healthcare settings, regardless of aerosol generating procedure ²¹². For school health clinics, ASHRAE provided guidance ranging from 6–10 ACH ³³⁴, and equivalent ventilation rates are still being researched by the Epidemic Task Force. This is generally higher than the non-pandemic standards.

REHVA shows how increasing ventilation above 1L/s/m^2 can reduce airborne infection risk and that 4L/s/m^2 may be advisable as a lower bound in office meeting rooms or classrooms (corresponding to 5ACH) ⁴⁰. They classify maintenance of indoor CO₂ levels below 800 and 1,000ppm (given outdoor CO₂ level of 400ppm) as “good” and “acceptable” ventilation, respectively. WHO suggested 5–6 ACH for public buildings in the context of SARS-CoV-2 pandemic control ^{42,43}. This is similar to what has been suggested in the US for holding K–12 school during the pandemic with 6 ACH as ideal, 5–6 as excellent, 4–5 as good, and 3–4 as bare minimum ³⁸. Guidelines are expected to evolve as understanding of ventilation infection control effectiveness increases. Ventilation is considered a helpful control within the context of other layers of protection including, in the context of the COVID-19 pandemic, use of face masks, physical distancing, de-densifying indoor spaces, upgrading filters in central HVAC systems, using portable air cleaners, deploying UV, and considering air flow dynamics to reduce exposure to infectious aerosols.